

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup>:</b> <b>C07K 14/705, C12N 15/12, 15/62, A61K 38/17</b>	<b>A1</b>	<b>(11) International Publication Number: -</b> <b>WO 99/51641</b> <b>(43) International Publication Date:</b> 14 October 1999 (14.10.99)
<b>(21) International Application Number:</b> PCT/US99/07333 <b>(22) International Filing Date:</b> 2 April 1999 (02.04.99) <b>(30) Priority Data:</b> 60/080,671 3 April 1998 (03.04.98) US <b>(71) Applicant (for all designated States except US):</b> NPS PHARMACEUTICALS, INC. [US/US]; Suite 240, 420 Chipeta Way, Salt Lake City, UT 84108 (US). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> STORMANN, Thomas, M. [US/US]; 1327 E. Harrison, Salt lake City, UT 84105 (US). HAMMERLAND, Lance, G. [US/US]; 3201 South 400 East, Salt Lake City, UT 84010 (US). STORJOHANN, Laura, L. [US/US]; 2592 East Stanford, Salt Lake City, UT 84117 (US). BUSBY, James, G. [US/US]; 3256 East Del Verde, Salt Lake City, UT 84109 (US). GARRETT, James, E. [US/US]; 1584 East 3150 South, Salt Lake City, UT 84106 (US). SIMIN, Rachel, T. [US/US]; 1520 East Redondo Avenue, Salt Lake City, UT 84105 (US). <b>(74) Agent:</b> WARBURG, Richard, J.; Lyon & Lyon LLP, 4225 Executive Square, La Jolla, CA 92037 (US).	<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
<b>(54) Title:</b> G-PROTEIN FUSION RECEPTORS AND CHIMERIC GABA <sub>B</sub> RECEPTORS  <b>(57) Abstract</b> <p>The present invention features G-protein fusion receptors and chimeric GABA<sub>B</sub> receptors (GABA<sub>B</sub>Rs), nucleic acid encoding such receptors, and the use of such receptors and nucleic acid. G-protein fusion receptors comprise at least one domain from a CaR, a mGluR, and/or a GABA<sub>B</sub> receptor fused directly or through a linker to a guanine nucleotide-binding protein (G-protein). Chimeric GABA<sub>B</sub>Rs comprise at least one of a GABA<sub>B</sub>R extracellular domain, a GABA<sub>B</sub>R transmembrane domain, or a GABA<sub>B</sub>R intracellular domain and one or more domains from a mGluR subtype 8 (mGluR8) and/or a CaR.</p>		

Applicants: Kenneth A. Jones, et al.

U.S. Serial No. : 09/211,755

Filed: December 15, 1998

Exhibit 6

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

DESCRIPTIONG-PROTEIN FUSION RECEPTORS AND CHIMERIC GABA<sub>A</sub> RECEPTORSRELATED APPLICATIONS

5 The present application claims priority to Garrett et al. U.S. Serial No. 60/080,671, filed April 3, 1998, which is hereby incorporated by reference herein in its entirety including the drawings.

FIELD OF THE INVENTION

10 The present invention relates to a G-protein fusion receptors, chimeric GABA<sub>A</sub> ( $\gamma$ -aminobutyric acid) receptors, nucleic acid encoding such receptors, and uses of such  
15 receptors and nucleic acid encoding such receptors.

BACKGROUND

The references cited herein are not admitted to be prior art to the claimed invention.

20 Chimeric receptors made up of peptide segments from different receptors have different uses such as being used to assess the functions of different sequence regions and to assess the activity of different compounds at a particular receptor. Examples of using chimeric receptors to assess the activity of  
25 different compounds are provided by Dull et al., U.S. Patent No. 4,859,609, Dull et al., U.S. Patent No. 5,030,576, and Fuller et al., International Application No. PCT/US96/12336, International Publication No. WO 97/05252.

Dull et al. U.S. Patent No. 4,859,609, and Dull et al. U.S.  
30 Patent No. 5,030,576, indicate the production and use of chimeric receptors comprising a ligand binding domain of a predetermined receptor and a heterologous reporter polypeptide. The Dull et al. patents provide as examples of chimerics: (1) a chimeric  
35 receptor made up of the insulin receptor extracellular  $\alpha$  chain, and the EGF receptor transmembrane and cytoplasmic domains without any HIR B-chain sequence; and (2) a hybrid receptor made

up of the v-erbB oncogene product intracellular domain fused to the EGF receptor extracellular and transmembrane domains.

Fuller et al. International Publication No. WO 97/05252 feature chimeric receptors made up of metabotropic glutamate receptor (mGluR) domains and calcium receptor (CaR) domains. The chimeric receptors allow the coupling of functional aspects of a mGluR with a CaR.

An example of the use of chimeric receptors to assess the functions of different sequence regions receptors are found in studies identifying regions of different guanine nucleotide-binding protein coupled receptors important for guanine nucleotide-binding protein coupling. (See, Kobilka et al., *Science* 240:1310-1316, 1988; Wess et al., *FEBS Lett.* 258:133-136, 1989; Cotecchia et al., *Proc. Natl. Acad. Sci. USA* 87:2896-2900, 1990; Lechleiter et al., *EMBO J.* 9:4381-4390, 1990; Wess et al., *Mol. Pharmacol.* 38:517-523, 1990; and Pin et al., *EMBO J.* 13:342-348, 1994.)

#### SUMMARY OF THE INVENTION

The present invention features G-protein fusion receptors and chimeric GABA<sub>B</sub> receptors (GABA<sub>B</sub>Rs), nucleic acid encoding such receptors, and the use of such receptors and nucleic acid. G-protein fusion receptors comprise at least one domain from a CaR, a mGluR, and/or a GABA<sub>B</sub> receptor fused directly or through a linker to a guanine nucleotide-binding protein (G-protein). Chimeric GABA<sub>B</sub>Rs comprise at least one of a GABA<sub>B</sub>R extracellular domain, a GABA<sub>B</sub>R transmembrane domain, or a GABA<sub>B</sub>R intracellular domain and one or more domains from a mGluR subtype 8 (mGluR8) and/or a CaR.

G-proteins are peripheral membrane proteins made up of an  $\alpha$  subunit, a  $\beta$  subunit, and a  $\gamma$  subunit. G-proteins interconvert between a GDP bound and a GTP bound form. Different types of G-proteins can affect different enzymes, such as adenylate cyclase and phospholipase-C.

Thus, a first aspect of the present invention describes a G-protein fusion receptor comprising:



an extracellular domain comprising an extracellular domain amino acid sequence substantially similar to either an extracellular CaR amino acid sequence, an extracellular mGluR amino acid sequence, or an extracellular GABA<sub>A</sub> receptor amino acid sequence;

5 a transmembrane domain joined to the carboxy terminus of said extracellular domain, said transmembrane domain comprising a transmembrane domain amino acid sequence substantially similar to either a transmembrane CaR amino acid sequence, a transmembrane mGluR amino acid sequence, or a transmembrane GABA<sub>A</sub> receptor amino acid sequence;

10 an intracellular domain joined to the carboxy terminus of said transmembrane domain comprising all or a portion of an intracellular amino acid sequence substantially similar to either an intracellular CaR amino acid sequence, an intracellular mGluR amino acid sequence, or an intracellular GABA<sub>A</sub> receptor amino acid sequence, provided that said portion is at least about 10 amino acids;

an optionally present linker joined to the carboxy terminus of said intracellular domain; and

20 a G-protein joined either to said intracellular domain or to said optionally present linker, provided that said G-protein is joined to said optionally present linker when said optionally present linker is present.

25 "Substantially similar" refers to at least 40% sequence similarity between respective polypeptide regions making up a domain. In preferred embodiments, substantially similar refers to at least 50%, at least 75%, at least 90%, at least 95% sequence similarity, or 100% (the same sequence), between polypeptide domains. The degree to which two polypeptide domains are substantially similar is determined by comparing the amino acid sequences located in corresponding domains. Sequence similarity is preferably determined using BLASTN (Altschul et al., *J. Mol. Biol.* 215:403-410, 1990).

30 The different receptor components of the G-protein receptor can come from the same receptor protein or from a chimeric receptor made up of different receptor domains. By swapping different domains compounds able to effect different domains of a

particular receptor can be identified and the activity of different compounds at different domains can be measured.

In different embodiments the CaR region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of the human CaR; mGluR region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of a human mGluR; and GABA<sub>B</sub>R region(s) present in the G-protein fusion are substantially similar to, comprise, or consist of portion(s) of a human GABA<sub>B</sub>R receptor.

In preferred embodiments concerning GABA<sub>B</sub>R regions that are present: the GABA<sub>B</sub>R extracellular domain is substantially similar to a GABA<sub>B</sub>R extracellular domain provided in SEQ. ID. NOS. 2-4; the GABA<sub>B</sub>R transmembrane domain is substantially similar to the GABA<sub>B</sub>R transmembrane domain provided in SEQ. ID. NOS. 7-9; and the GABA<sub>B</sub>R intracellular domain is substantially similar to a GABA<sub>B</sub>R intracellular domain provided in SEQ. ID. NOS. 12-14.

In preferred embodiments concerning CaR regions that are present: the CaR extracellular domain is substantially similar to the CaR extracellular provided in SEQ. ID. NO. 1; the CaR transmembrane domain is substantially similar to the CaR transmembrane domain provided in SEQ. ID. NO. 6; and the CaR intracellular domain is substantially similar to the CaR intracellular domain such as that provided in SEQ. ID. NO. 11.

Various different mGluR subtypes present in different organisms, including humans, are described in different patent publications as follows: mGluR<sub>1</sub> - WO 94/29449, EP 569 240 A1, WO 92/10583 and U.S. Patent No. 5,385,831; mGluR<sub>2</sub> - WO 94/29449, WO 96/06167, and EP 711 832 A2; mGluR<sub>3</sub> - WO 94/29449, and WO 95/22609; mGluR<sub>4</sub> - WO 95/08627, WO 95/22609, and WO 96/29404; mGluR<sub>5</sub> - WO 94/29449; mGluR<sub>6</sub> - WO 95/08627; mGluR<sub>7</sub> - U.S. Patent No. 5,831,047, WO 95/08627 and WO 96/29404; and mGluR<sub>8</sub> - WO 97/48724 and EP 816 498 A2. (Each of these references are hereby incorporated by reference herein.)

In preferred embodiments concerning mGluR regions that are present: the mGluR extracellular domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human

mGluR 8; the mGluR transmembrane domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human mGluR 8; and the mGluR intracellular domain is substantially similar to either human mGluR 1, human mGluR 2, human mGluR 3, human mGluR 4, human mGluR 5, human mGluR 6, human mGluR 7, or human mGluR 8.

Another aspect of the present invention describes a nucleic acid comprising a nucleotide sequence encoding for a G-protein fusion receptor.

Another aspect of the present invention describes a recombinant cell comprising an expression vector encoding for a G-protein fusion receptor, and a cell where the G-protein fusion receptor is expressed. Preferably, the G-protein fusion receptor is functional in the cell.

Another aspect of the present invention describes a recombinant cell produced by combining (a) a cell where a G-protein fusion receptor is expressed, and (b) a vector comprising nucleic acid encoding a G-protein fusion receptor and elements for introducing heterologous nucleic acid into the cell. Preferably, the G-protein fusion receptor is functional in the cell.

Another aspect of the present invention describes a process for the production of a G-protein fusion receptor. The process is performed by growing host cells comprising a G-protein fusion receptor.

Another aspect of the present invention describes a method of measuring the ability of a compound to affect G-protein fusion receptor activity.

Another aspect of the present invention describes a chimeric GABA<sub>B</sub>R comprising an extracellular domain, a transmembrane domain and an intracellular domain, wherein at least one domain is from a GABA<sub>B</sub>R and at least one domain is from CaR or mGluR8. The extracellular domain comprises an amino acid sequence substantially similar to a CaR extracellular domain (SEQ. ID. NO.

1), a GABA<sub>A</sub>R1a extracellular domain (SEQ. ID. NO. 2), a GABA<sub>A</sub>R1b extracellular domain (SEQ. ID. NO. 3), a GABA<sub>A</sub>R2 extracellular domain (SEQ. ID. NO. 4), or a mGluR8 extracellular domain (SEQ. ID. NO. 5).

5       The transmembrane domain comprises an amino acid sequence substantially similar to a CaR transmembrane domain (SEQ. ID. NO. 6), a GABA<sub>A</sub>R1a transmembrane domain (SEQ. ID. NO. 7), a GABA<sub>A</sub>R1b transmembrane domain (SEQ. ID. NO. 8), a GABA<sub>A</sub>R2 transmembrane domain (SEQ. ID. NO. 9), or a mGluR8 transmembrane domain (SEQ. ID. NO. 10).

10       The intracellular domain comprises an amino acid sequence substantially similar to a CaR intracellular domain (SEQ. ID. NO. 11), a GABA<sub>A</sub>R1a intracellular domain (SEQ. ID. NO. 12), a GABA<sub>A</sub>R1b intracellular domain (SEQ. ID. NO. 13), a GABA<sub>A</sub>R2 intracellular domain (SEQ. ID. NO. 14), or a mGluR8 intracellular domain (SEQ. ID. NO. 15).

15       Preferred chimeric GABA<sub>A</sub>Rs contain at least one mGluR8 intracellular, transmembrane or extracellular domain, or at least one CaR intracellular, transmembrane or extracellular domain.

20       More preferably, the chimeric GABA<sub>A</sub>R contains at least one CaR domain.

      In preferred embodiments concerning mGluR8 regions that are present: the mGluR8 extracellular domain is substantially similar to the mGluR8 extracellular domain provided in SEQ. ID. NO. 5;

25       the mGluR8 transmembrane domain is substantially similar to the mGluR8 transmembrane domain provided in SEQ. ID. NO. 10; and the mGluR8 intracellular domain is substantially similar to the mGluR8 receptor intracellular provided in SEQ. ID. NO. 15.

      Preferably, the domains are functionally coupled such that a

30       signal from the binding of an extracellular ligand is transduced to the intracellular domain when the chimeric receptor is present in a suitable host cell. A suitable host cell contains the elements for functional signal transduction for receptors coupled to a G-protein.

Another aspect of the present invention describes a nucleic acid comprising a nucleotide sequence encoding for a chimeric GABA<sub>A</sub>R.

Another aspect of the present invention describes a recombinant cell comprising an expression vector encoding for a chimeric GABA<sub>A</sub>R, and a cell where the chimeric GABA<sub>A</sub>R is expressed. Preferably, the chimeric GABA<sub>A</sub>R is functional in the cell.

Another aspect of the present invention describes a recombinant cell produced by combining (a) a cell where a chimeric GABA<sub>A</sub>R is expressed, and (b) a vector comprising nucleic acid encoding the chimeric GABA<sub>A</sub>R and elements for introducing heterologous nucleic acid into the cell. Preferably, the chimeric GABA<sub>A</sub>R is functional in the cell.

Another aspect of the present invention describes a process for the production of a chimeric receptor. The process is performed by growing host cells comprising a chimeric GABA<sub>A</sub>R.

Another aspect of the present invention describes a method of measuring the ability of a compound to affect GABA<sub>A</sub>R or mGluR activity. The method is performed by measuring the ability of a compound to affect chimeric GABA<sub>A</sub>R or mGluR activity.

Another aspect of the present invention describes a fusion receptor polypeptide comprising a receptor and a G-protein  $\alpha$  subunit, wherein said G-protein  $\alpha$  subunit is fused to the intracellular domain of said receptor, provided that the receptor is not an adrenoceptor.

Various examples are described herein. These examples are not intended in any way to limit the claimed invention.

Other features and advantages of the invention will be apparent from the following drawings, the description of the invention, the examples, and the claims.

BRIEF DESCRIPTION OF DRAWINGS

Figures 1a-1d illustrate the amino acid sequences of a human CaR extracellular domain (SEQ. ID. NO. 1), a human GABA<sub>B</sub>R1a extracellular domain (SEQ. ID. NO. 2), a human GABA<sub>B</sub>R1b extracellular domain (SEQ. ID. NO. 3), a human GABA<sub>B</sub>R2 extracellular domain (SEQ. ID. NO. 4), and a human mGluR8 extracellular domain (SEQ. ID. NO. 5).

Figures 2a-2b illustrate the amino acid sequences of a human CaR transmembrane domain (SEQ. ID. NO. 6), a human GABA<sub>B</sub>R1a transmembrane domain (SEQ. ID. NO. 7), a human GABA<sub>B</sub>R1b transmembrane domain (SEQ. ID. NO. 8), a human GABA<sub>B</sub>R2 transmembrane domain (SEQ. ID. NO. 9), and a human mGluR8 transmembrane domain (SEQ. ID. NO. 10).

Figures 3a-3b illustrate the amino acid sequences of a human CaR intracellular domain (SEQ. ID. NO. 11), a human GABA<sub>B</sub>R1a intracellular domain (SEQ. ID. NO. 12), a human GABA<sub>B</sub>R1b intracellular domain (SEQ. ID. NO. 13), a human GABA<sub>B</sub>R2 intracellular domain (SEQ. ID. NO. 14), and a human mGluR8 intracellular domain (SEQ. ID. NO. 15).

Figures 4a-4b illustrate the amino acid sequence of G $\alpha_{15}$  (SEQ. ID. NO. 16) and G $\alpha_{16}$  (SEQ. ID. NO. 17).

Figures 5a-5r illustrate the cDNA sequences encoding for human CaR (SEQ. ID. NO. 18), human GABA<sub>B</sub>R1a (SEQ. ID. NO. 19), human GABA<sub>B</sub>R1b (SEQ. ID. NO. 20), and human GABA<sub>B</sub>R2 (SEQ. ID. NO. 21).

Figures 6a-6h illustrate the cDNA sequence for rat GABA<sub>B</sub>R1a (SEQ. ID. NO. 22) and rat GABA<sub>B</sub>R1b (SEQ. ID. NO. 23).

Figures 7a-7c illustrate the amino sequence for rat GABA<sub>B</sub>R1a (SEQ. ID. NO. 24) and rat GABA<sub>B</sub>R1b (SEQ. ID. NO. 25).

Figure 8 illustrates the ability of a chimeric CaR/GABA<sub>B</sub>R2 (CaR extracellular and transmembrane domains, and intracellular GABA<sub>B</sub>R2 domain) to transduce a signal. Signal production was measured by detecting an increase in the calcium-activated chloride current. The line in the middle of the increase signifies a wash step.

Figures 9a-9p illustrate the cDNA sequence for human mGluR2

(SEQ. ID. NO. 26), chimeric hCAR/hmGluR2 (SEQ. ID. NO. 30), chimeric hmGluR2/hCaR (SEQ. ID. NO. 34), and chimeric hmGluR8/hCaR (SEQ. ID. NO. 38).

5       Figures 10a-10f illustrate the amino acid sequence for human mGluR2 (SEQ. ID. NO. 27), chimeric hCAR/hmGluR2 (SEQ. ID. NO. 31), chimeric hmGluR2/hCaR (SEQ. ID. NO. 35), chimeric hmGluR8/hCaR (SEQ. ID. NO. 39).

10       Figures 11a-11v illustrate the cDNA sequence for the phCaR/hmGluR2\*Gqi5 fusion construct (SEQ. ID. NO. 32), pmGluR2//CaR\*G $\alpha$ i5 fusion construct (SEQ. ID. NO. 36), pmGluR2//CaR\*G $\alpha$ i5+3Ala linker fusion construct (SEQ. ID. NO. 46), and the mGluR8//CaR\*G $\alpha$ i5 fusion construct (SEQ. ID. NO. 40).

15       Figures 12a-12h illustrate the amino acid sequence for the phCaR/hmGluR2\*Gqi5 fusion construct (SEQ. ID. NO. 33), pmGluR2//CaR\*G $\alpha$ i5 fusion construct (SEQ. ID. NO. 37), pmGluR2//CaR\*G $\alpha$ i5+3Ala linker fusion construct (SEQ. ID. NO. 47), and the mGluR8//CaR\*G $\alpha$ i5 fusion construct (SEQ. ID. NO. 41).

20       Figures 13a-13m illustrate the cDNA sequence for the GABA-R2\*Gqo5 fusion construct (SEQ. ID. NO. 42) and the GABA-BR1a\*Gqo5 fusion construct (SEQ. ID. NO. 44).

25       Figures 14a-14e illustrates the amino acid sequence for the GABA-BR2\*Gqo5 fusion construct (SEQ. ID. NO. 43) and the GABA-BR1a\*Gqo5 fusion construct (SEQ. ID. NO. 45).

30       Figure 15 illustrates the ability of different G-protein fusions to transduce signal resulting from ligand binding. mGluR2//CaR\*Gqi5 is shown by SEQ. ID. NO. 37, CaR/mGluR2\*Gqi5 is shown by SEQ. ID. NO. 33, mGluR8//CaR\*Gqi5 is shown by SEQ. ID. NO. 41.

#### DETAILED DESCRIPTION OF THE INVENTION

35       The CaR, mGluR, and the GABA<sub>A</sub>R are structurally similar in that they are each a single subunit membrane protein possessing an extracellular domain, a transmembrane domain comprising seven putative membrane spanning helices connected by three intracellular and three extracellular loops, and an intracellular

carboxy-terminal domain. Signal transduction is activated by the extracellular binding of an agonist. The signal is transduced to the intracellular components of the receptor causing an intracellular effect.

5       Signal transduction from agonist binding to an extracellular region can be modulated by compounds acting at a downstream transmembrane domain or the intracellular domain. Downstream effects include antagonist actions of compounds and allosteric actions of compounds.

10       The transmembrane domain provides different types of target sites for compounds modulating receptor activity in different environments. As noted above, the transmembrane domain contains extracellular, transmembrane, and intracellular components.

15       Compounds modulating GABA<sub>A</sub>R, CaR, or mGluR activity can be obtained, for example, by screening a group or library of compounds to identify those compounds having the desired activity and then synthesizing such compound. Thus, included in the present invention is a method of making a GABA<sub>A</sub>R, CaR, or mGluR active compound by first screening for a compound having desired

20       properties and then chemically synthesizing that compound.

#### Metabotropic Glutamate Receptors (mGluRs)

mGluRs are G protein-coupled receptors capable of activating a variety of intracellular secondary messenger systems following the binding of glutamate (Schoepp et al., *Trends Pharmacol. Sci.* 11:508, 1990; Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993, hereby incorporated by reference herein).

25       the binding of glutamate (Schoepp et al., *Trends Pharmacol. Sci.* 11:508, 1990; Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993, hereby incorporated by reference herein).

Activation of different mGluR subtypes in situ elicits one or more of the following responses: activation of phospholipase C, increases in phosphoinositide (PI) hydrolysis, intracellular calcium release, activation of phospholipase D, activation or inhibition of adenylyl cyclase, increases and decreases in the formation of cyclic adenosine monophosphate (cAMP), activation of guanylyl cyclase, increases in the formation of cyclic guanosine monophosphate (cGMP), activation of phospholipase A<sub>2</sub>, increases in

30       increases in phosphoinositide (PI) hydrolysis, intracellular calcium release, activation of phospholipase D, activation or inhibition of adenylyl cyclase, increases and decreases in the formation of cyclic adenosine monophosphate (cAMP), activation of guanylyl cyclase, increases in the formation of cyclic guanosine monophosphate (cGMP), activation of phospholipase A<sub>2</sub>, increases in

35       monophosphate (cGMP), activation of phospholipase A<sub>2</sub>, increases in



arachidonic acid release, and increases or decreases in the activity of voltage- and ligand-gated ion channels (Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993; Schoepp, *Neurochem. Int.* 24:439, 1994; Pin and Duvoisin, *Neuropharmacology* 34:1, 1995, hereby incorporated by reference herein).

5 Eight distinct mGluR subtypes have been isolated. (Nakanishi, *Neuron* 13:1031, 1994; Pin and Duvoisin, *Neuropharmacology* 34:1, 1995; Knopfel et al., *J. Med. Chem.* 38:1417; *Eur. J. Neuroscience* 7:622-629, 1995, each of these references is hereby incorporated  
10 by reference herein.) The different mGluRs possess a large amino-terminal extracellular domain (ECD) followed by seven putative transmembrane domain (7TMD) comprising seven putative membrane spanning helices connected by three intracellular and three  
15 extracellular loops, and an intracellular carboxy-terminal domain of variable length (cytoplasmic tail).

Human mGluR8 is described by Stormann et al., International Application Number PCT/US97/09025, International Publication Number WO 97/48724, and mouse mGluR8 is described by Duvoisin et al., *J. Neurosci.* 15:3075-3083, 1995, (both of these references  
20 are hereby incorporated by reference herein). mGluR8 couples to  $G_i$ . Agonists of mGluR8 include L-glutamate and L-2-amino-4-phosphonobutyrate.

mGluR8 activity can be measured using standard techniques. For example,  $G_i$  negatively couples to adenylate cyclase to inhibit  
25 intracellular cAMP accumulation in a pertussis toxin-sensitive fashion. Thus, mGluR8 activity can be measured, for example, by measuring inhibition of forskolin-stimulated cAMP production as described by Duvoisin et al., *J. Neurosci.* 15:3075-3083, 1995.

mGluRs have been implicated in a variety of neurological  
30 pathologies. Examples of such pathologies include stroke, head trauma, spinal cord injury, epilepsy, ischemia, hypoglycemia, anoxia, and neurodegenerative diseases such as Alzheimer's disease (Schoepp and Conn, *Trends Pharmacol. Sci.* 14:13, 1993; Cunningham et al., *Life Sci.* 54: 135, 1994; Pin et al.,  
35 *Neuropharmacology* 34:1, 1995; Knopfel et al., *J. Med. Chem.*

38:1417, 1995, each of which is hereby incorporated by reference herein).

#### Calcium Receptor

5       The CaR responds to changes of extracellular calcium concentration and also responds to other divalent and trivalent cations. The CaR is a G-protein coupled receptor containing an extracellular  $\text{Ca}^{2+}$  binding domain. Activation of the CaR, descriptions of CaRs isolated from different sources, and  
10       examples of CaR active compound are provided in Nemeth NIPS 10:1-5, 1995, Brown et al. U.S. Patent No. 5,688,938, Van Wagenen et al., International Application Number PCT/US97/05558 International Publication Number WO 97/37967, Brown E.M. et al., Nature 366:575, 1993, Riccardi D., et al., Proc. Nat'l. Acad.  
15       Sci. USA 92:131-135, 1995, and Garrett J.E., et al., J. Biol. Chem. 31:12919-12925, 1995. (Each of these references are hereby incorporated by reference herein.) Brown et al. U.S. Patent No. 5,688,938 and Van Wagenen et al., International Application  
20       Number PCT/US97/05558 International Publication Number WO 97/37967, describe different types of compounds active at the CaR including compounds which appear to be allosteric modulators and CaR antagonists.

      The CaR can be targeted to achieve therapeutic effects. Examples of target diseases are provided in Brown et al. U.S.  
25       Patent No. 5,688,938, and Van Wagenen et al., International Application Number PCT/US97/05558 International Publication Number WO 97/37967, and include hyperparathyroidism and osteoporosis.

#### $\gamma$ -Aminobutyric acid Receptors ( $\text{GABA}_\text{A}$ Rs)

30        $\text{GABA}_\text{A}$ Rs are G-protein coupled metabotropic receptors.  $\text{GABA}_\text{A}$ Rs modulate synaptic transmission by inhibiting presynaptic transmitter release and by increasing  $\text{K}^+$  conductance responsible for long-lasting inhibitory postsynaptic potentials. (See,

Kaupmann et al., *Nature* 386:239-246, 1997, hereby incorporated by reference herein.)

GABA<sub>A</sub>Rs are found in the mammalian brain, in locations outside of the brain, and in lower species. Outside of the brain, GABA<sub>A</sub>Rs have been identified on axon terminals and ganglion cell bodies of the autonomic nervous system, on fallopian tube and uterine intestinal smooth muscle cells, in the kidney cortex, urinary bladder muscle and on testicular interstitial cells. (See, Bowery, *Annu. Rev. Pharmacol. Toxicol.* 33:109-147, 1993, hereby incorporated by reference herein.)

Different GABA<sub>A</sub>Rs subtypes exist. Kaupmann et al., *Nature* 386:239-246, 1997, indicate that they cloned GABA<sub>A</sub>Rs. Nucleic acid encoding two GABA<sub>A</sub>R proteins were indicated to be cloned from rat brain: GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b. GABA<sub>A</sub>R1a differs from GABA<sub>A</sub>R1b in that the N-terminal 147 residues are replaced by 18 amino acids. GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b appear to be splice variants. The cloned GABA<sub>A</sub>Rs were indicated to negatively couple adenylyl cyclases and show sequence similarity to the metabotropic receptors for L-glutamate (mGluR). Northern blot analysis indicated that GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b is present in brain and testis, but not in kidney, skeletal muscle, liver, lung, spleen, or heart.

Kaupmann et al., International Application Number PCT/EP97/01370, International Publication Number WO 97/46675, indicate that they have obtained rat GABA<sub>A</sub>R clones, GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b; and humans GABA<sub>A</sub>R clones, GABA<sub>A</sub>R1a/b (representing a partial receptor clone) and GABA<sub>A</sub>R1b (representing a full-length receptor clone). Amino acid sequence information, and encoding cDNA sequence information, is provided for the different GABA<sub>A</sub>R clones.

Another GABA<sub>A</sub>R subtype is GABA<sub>A</sub>R2. Northern blot analysis reveals that an approximately 6.3 Kb human GABA<sub>A</sub>R2 transcript is abundantly expressed in the human brain. Expression is not detected in the heart, placenta, lung, liver, skeletal muscle, kidney and pancreas under conditions where GABA<sub>A</sub>R2 transcript was

identified in the human brain. Within the human brain GABA<sub>B</sub>R2 is broadly expressed at variable levels.

GABA<sub>B</sub>R functions as a heterodimer of the subunits GABA<sub>B</sub>R1 or GABA<sub>B</sub>R2. (Jones et al. *Nature* 396:674-679, 1998, hereby  
5 incorporated by reference herein.)

GABA<sub>B</sub>Rs have been targeted to achieve therapeutic effects. Kerr and Ong, *DDT* 1:371-380, 1996, describe different compounds indicated to be GABA<sub>B</sub>R agonists and GABA<sub>B</sub>R antagonists. Kerr and Ong also review therapeutic implications of affecting GABA<sub>B</sub>R  
10 activity including, spasticity and motor control, analgesia, epilepsy, cognitive effects, psychiatric disorders, alcohol dependence and withdrawal, feeding behavior, cardiovascular and respiratory functions, and peripheral functions.

Bittiger et al., *Tips* 4:391-394, 1993, review therapeutic  
15 applications of GABA<sub>B</sub>R antagonists. Potential therapeutic applications noted by Bittiger et al. include cognitive processes, epilepsy, and depression.

#### G-Protein Fusion Receptors

20 Examples of some different types of G-protein fusion receptors, and advantages of some receptors, are provided below. Using the present application as guide additional G-protein receptors fusion can be constructed.

G-protein fusion receptors contain an intracellular domain  
25 of a receptor fused to a G-protein  $\alpha$  subunit ( $G_{\alpha}$ ).  $G_{\alpha}$  fusions to adrenoceptors have been reported by Bertin et al., *Receptors and Channels* 5:41-51, 1997; Wise and Milligan, *Journal of Biological Chemistry* 39:24673-24678, 1997; and Bertin et al., *Proc. Natl. Acad. Sci. USA* 91:8827-8831, 1994 (each of which are  
30 hereby incorporated by reference herein). These studies were indicated to produce a functional chimeric by fusing the  $\alpha_{2A}$ -adrenoceptor to the  $G_{11\alpha}$ , or the  $\beta_2$ -adrenoceptor to the  $G_{s\alpha}$ .

The G-protein fusion receptors described by the present invention include a G-protein fused to an intracellular domain,  
35 where the intracellular domain when present in a wild type

receptor does not interact with that type of G-protein. Thus, the present invention also describes swapping of signals by fusing an intracellular domain to a  $G_{\alpha}$  normally not coupled to that intracellular domain. The use of such fusion proteins, while applicable to chimeric GABA<sub>A</sub>Rs, is not limited to chimeric GABA<sub>A</sub>Rs. Indeed, such technology can be applied to receptors containing an extracellular domain, transmembrane domain and intracellular domain of a wild type receptor.

Preferred G-proteins fusion receptors contain an intracellular domain fused to a promiscuous  $G_{\alpha}$  that couples to phospholipase C resulting in the mobilization of intracellular calcium. Increases in intracellular calcium can be conveniently measured through the use of dyes. Such techniques are well known in the art and are described, for example by Brown et al. U.S. Patent No. 5,688,938.

In an embodiment G-proteins fusions can also be used to decrease receptor desensitization.

Examples of promiscuous  $G_{\alpha}$ 's coupling to phospholipase C include naturally occurring G-proteins such as  $G_{\alpha_{15}}$  and  $G_{\alpha_{16}}$ , and chimeric G-protein such as Gqo5 and Gqi5. Gqo5 and Gqi5 are made of a Gq portion where the five amino acids at the C-terminal are from either  $G_o$  or  $G_i$ , respectively (Conklin et al., *Nature* 363:274-277, 1993, hereby incorporated by reference herein). The Gq portion of such chimeric receptors provides for phospholipase C coupling while the terminal  $G_o$  or  $G_i$  portion allows the chimeric G-protein to couple to different receptor proteins that are normally involved in inhibitor effects on adenylate cyclase.

In an embodiment of the present invention the employed G-protein is from a human source or is made up of different G-protein components each from a human source.

G-proteins fusions can be created, for example, by fusing directly or indirectly the intracellular domain of a receptor protein to a polypeptide having an amino acid sequence substantially similar to  $G_{\alpha_{15}}$ ,  $G_{\alpha_{16}}$ , Gqo5 or Gqi5. In different embodiments, the receptor is fused directly or indirectly to a G-

protein consisting of the amino acid sequence of  $G_{\alpha 15}$ ,  $G_{\alpha 16}$ ,  $G_{qo5}$  or  $G_{qi5}$ .

The intracellular domain portion of a receptor protein fused directly or indirectly to a G-protein should be at least about 10 amino acids in length. In different embodiments the portion is at least about 50 amino acids, at least about 100 amino acids, or the full length of an intracellular domain.

The intracellular domain can be directly linked to a G-protein or can be indirectly linked through an optionally present linker. Optionally present linkers are preferably about 3 to about 30 amino acids in length. Preferred linkers are made up of alanine, glycine, or a combination thereof.

#### Chimeric Receptors

Examples of some different types of chimeric receptors, and advantages of some receptors, are provided below. Using the present application as guide additional chimeric receptors can be constructed.

#### 20 Chimeric GABA<sub>A</sub>R Extracellular Domain

Chimeric GABA<sub>A</sub>Rs containing a GABA<sub>A</sub>R extracellular domain are particularly useful for studying the importance of the GABA<sub>A</sub>R extracellular domain and assaying for compounds active at the extracellular domain. Preferably chimeric GABA<sub>A</sub>Rs containing a GABA<sub>A</sub>R extracellular domain also contain a CaR intracellular domain.

A variety of different activities have been generally attributed to GABA<sub>A</sub>R subtypes. (E.g., Kerr and Ong, DDT 1:371-380, 1996.) Kaupmann et al., Nature 386:239-246, 1997, report that in preliminary experiments involving GABA<sub>A</sub>R1a they did not detect positive coupling to the adenylyl cyclase or coupling to the phospholipase effector system.

An intracellular CaR domain can be used to couple with G-proteins which activate phospholipase C and mobilize intracellular calcium. Mobilization of intracellular calcium is

readily detected, for example, by fluorescent indicators of intracellular  $\text{Ca}^{2+}$ .

An additional advantage of using the intracellular CaR domain is that CaR G-protein activation is not rapidly desensitized. Thus, the intracellular CaR domain can be used to produce a stronger intracellular signal than a signal produced from a receptor which is desensitized rapidly.

More preferably, the chimeric  $\text{GABA}_\text{B}\text{R}$  contains an intracellular CaR domain, and also contains either a CaR or a  $\text{GABA}_\text{B}\text{R}$  transmembrane domain. Advantages of using a CaR transmembrane domain include separating the effects occurring at a  $\text{GABA}_\text{B}\text{R}$  extracellular domain from effects occurring at a transmembrane domain; and providing additional intracellular elements, present on transmembrane intracellular loops, useful for coupling to G-protein.

A  $\text{GABA}_\text{B}\text{R}$  transmembrane domain is useful for examining whether the transmembrane  $\text{GABA}_\text{B}\text{R}$  can be targeted to affect  $\text{GABA}_\text{B}\text{R}$  activity, and obtaining compounds active at the  $\text{GABA}_\text{B}\text{R}$  transmembrane domain. For example, a transmembrane  $\text{GABA}_\text{B}\text{R}$  can be used to screen for transmembrane allosteric modulators and antagonists.

#### Chimeric $\text{GABA}_\text{B}\text{R}$ Transmembrane Domain

Chimeric  $\text{GABA}_\text{B}\text{Rs}$  containing a  $\text{GABA}_\text{B}\text{R}$  transmembrane are particularly useful for studying the importance of the  $\text{GABA}_\text{B}\text{R}$  transmembrane domain and assaying for compounds active at the transmembrane domain. Preferably Chimeric  $\text{GABA}_\text{B}\text{Rs}$  containing a  $\text{GABA}_\text{B}\text{R}$  transmembrane domain contain an extracellular domain which is either mGluR8 or CaR, and an intracellular CaR domain.

More preferably, the chimeric  $\text{GABA}_\text{B}\text{R}$  contains an extracellular domain from either mGluR8 or CaR, a  $\text{GABA}_\text{B}\text{R}$  transmembrane, and an intracellular CaR domain. A chimeric  $\text{GABA}_\text{B}\text{R}$  containing extracellular mGluR8 or CaR domains can readily be stimulated using mGluR8 or CaR ligands.

Chimeric GABA<sub>A</sub>R Intracellular Domain

Chimeric GABA<sub>A</sub>Rs containing a GABA<sub>A</sub>R intracellular domain are particularly useful for studying the importance of the GABA<sub>A</sub>R intracellular domain and assaying for compounds active at the intracellular domain. Preferably, the chimeric receptors contain an extracellular domain from either mGluR8 or CaR. The extracellular mGluR8 or CaR domains can readily be activated using mGluR8 or CaR ligands.

Receptor Domains

Domains of a G-protein fusion receptor, a chimeric receptor, and G<sub>q</sub>, substantially similar to a particular sequence can be readily produced using the disclosure provided herein in conjunction with information well known in the art. Substantially similar sequences can be obtained taking into account sequence information for a particular type of receptor obtained from different sources, different types of amino acids which are to some extent interchangeable, and the ease of experimentation with which functional receptor activity can be assayed.

Substantially similar sequences includes amino acid alterations such as deletions, substitutions, additions, and amino acid modifications. A "deletion" refers to the absence of one or more amino acid residue(s) in the related polypeptide. An "addition" refers to the presence of one or more amino acid residue(s) in the related polypeptide. Additions and deletions to a polypeptide may be at the amino terminus, the carboxy terminus, and/or internal. Amino acid "modification" refers to the alteration of a naturally occurring amino acid to produce a non-naturally occurring amino acid. A "substitution" refers to the replacement of one or more amino acid residue(s) by another amino acid residue(s) in the polypeptide. Derivatives can contain different combinations of alterations including more than one alteration and different types of alterations.



The sequences of polypeptides can be compared from different sources to help identify variable amino acids not essential for receptor activity. For example, Figure 7 provides the rat GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b amino acid sequences. The rat GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b amino acid sequences can be compared with the human GABA<sub>A</sub>R1a and GABA<sub>A</sub>R1b sequences to identify conserved and variable amino acids. Derivatives can then be produced where a variable amino acid is changed, and receptor activity can be readily tested.

10 Similarly, the amino acid sequences for CaR, mGluR8, and G-proteins from different sources are either known in the art or can readily be obtained. Examples of such references are provided above.

15 While the effect of an amino acid change varies depending upon factors such as phosphorylation, glycosylation, intra-chain linkages, tertiary structure, and the role of the amino acid in the active site or a possible allosteric site, it is generally preferred that a substituted amino acid is from the same group as the amino acid being replaced. To some extent the following groups contain amino acids which are interchangeable: the basic amino acids lysine, arginine, and histidine; the acidic amino acids aspartic and glutamic acids; the neutral polar amino acids serine, threonine, cysteine, glutamine, asparagine and, to a lesser extent, methionine; the nonpolar aliphatic amino acids 25 glycine, alanine, valine, isoleucine, and leucine (however, because of size, glycine and alanine are more closely related and valine, isoleucine and leucine are more closely related); and the aromatic amino acids phenylalanine, tryptophan, and tyrosine. In addition, although classified in different categories, alanine, 30 glycine, and serine seem to be interchangeable to some extent, and cysteine additionally fits into this group, or may be classified with the polar neutral amino acids.

While proline is a nonpolar neutral amino acid, its replacement represents difficulties because of its effects on 35 conformation. Thus, substitutions by or for proline are not

preferred, except when the same or similar conformational results can be obtained. The conformation conferring properties of proline residues may be obtained if one or more of these is substituted by hydroxyproline (Hyp).

5           Examples of modified amino acids include the following:

altered neutral nonpolar amino acids such as  $\omega$ -amino acids of the formula  $H_2N(CH_2)_nCOOH$  where  $n$  is 2-6, sarcosine (Sar), t-butylalanine (t-BuAla), t-butylglycine (t-BuGly), N-methyl isoleucine (N-MeIle), and norleucine (Nleu); altered neutral  
10 aromatic amino acids such as phenylglycine; altered polar, but neutral amino acids such as citrulline (Cit) and methionine sulfoxide (MSO); altered neutral and nonpolar amino acids such as cyclohexyl alanine (Cha); altered acidic amino acids such as cysteic acid (Cya); and altered basic amino acids such as  
15 ornithine (Orn).

Preferred derivatives have one or more amino acid alteration(s) which do not significantly affect the receptor activity of the related receptor protein. In regions of receptor domains not necessary for receptor activity, amino acids may be  
20 deleted, added or substituted with less risk of affecting activity. In regions required for receptor activity, amino acid alterations are less preferred as there is a greater risk of affecting receptor activity.

Derivatives can be produced using standard chemical  
25 techniques and recombinant nucleic acid techniques.

Modifications to a specific polypeptide may be deliberate, as through site-directed mutagenesis and amino acid substitution during solid-phase synthesis, or may be accidental such as through mutations in hosts which produce the polypeptide.

30 Polypeptides including derivatives can be obtained using standard techniques such as those described by Sambrook et al., *Molecular Cloning*, Cold Spring Harbor Laboratory Press (1989). For example, Chapter 15 of Sambrook describes procedures for site-directed mutagenesis of cloned DNA.

### Receptor Nucleic Acid

G-protein fusion and chimeric receptor nucleic acid can be produced based on the information provided herein along with standard recombinant nucleic acid techniques. Examples of references describing recombinant nucleic acid techniques include  
5 *Molecular Cloning*, Sambrook et al., Cold Spring Harbor Laboratory Press (1989); and *Current Protocols in Molecular Biology*, Frederick et al., John Wiley & Sons, Inc. (1995).

Due to the degeneracy of the genetic code different nucleic  
10 acid sequences can encode for a particular polypeptide. Thus, a large number of nucleic acids encoding for a receptor having the same amino acid sequence can be produced.

An embodiment of the present invention uses human nucleic acid encoding for the domains from CaR, GABA<sub>A</sub>R1A, GABA<sub>A</sub>R1B,  
15 GABA<sub>A</sub>R2 and/or mGluR8. The amino acid sequences of different domains is provided in Figures 1-3.

### Recombinant Cells

Nucleic acid expressing a functional G-Protein fusion or a  
20 chimeric receptor can be used to create transfected cells lines expressing such receptors. Such cell lines have a variety of uses such as being used for high-throughput screening for compounds modulating receptor activity; being used to assay binding to the receptor; and as factories to produce large  
25 amounts of a receptor.

A variety of cell lines can couple exogenously expressed receptors to endogenous functional responses. Cell lines such as NIH-3T3, HeLa, NG115, CHO, HEK 293 and COS7 which are expected to lack CaR, mGluR8, and GABA<sub>A</sub>R can be tested to confirm that they  
30 lack these receptors.

Production of stable transfectants can be accomplished by transfection of an appropriate cell line with, for example, an expression vector such as pMSG vector, in which the coding sequence for the G-protein fusion or chimeric GABA<sub>A</sub>R cDNA has been  
35 cloned. Expression vectors containing a promoter region, such as

the mouse mammary tumor virus promoter (MMTV), drive high-level transcription of cDNAs in a variety of mammalian cells. In addition, these vectors contain genes for selecting cells stably expressing cDNA of interest. The selectable marker in the pMSG  
5 vectors encode an enzyme, xanthine-guanine phosphoribosyl transferase (XGPRT), conferring resistance to a metabolic inhibitor that is added to the culture to kill nontransfected cells.

The most effective method for transfection of eukaryotic  
10 cell lines with plasmid DNA varies with the given cell type. The expression construct will be introduced into cultured cells by the appropriate technique, such as  $\text{Ca}^{2+}$  phosphate precipitation, DEAE-dextran transfection, lipofection or electroporation.

Expression of the receptor cDNA in cell lines can be  
15 assessed by solution hybridization and Northern blot analysis.

#### Binding Assays

The present invention also includes using G-protein fusion receptors or chimeric  $\text{GABA}_B\text{R}$  in a binding assay. G-protein fusion  
20 receptors or chimeric  $\text{GABA}_B\text{Rs}$  having a particular  $\text{GABA}_B\text{R}$  domain can be used, for example to facilitate obtaining compounds able to bind to that particular receptor domain; and to determine whether a compound which binds to a particular domain. For example, in a complete chimeric  $\text{GABA}_B\text{R}$  containing extracellular,  
25 transmembrane, and intracellular domains, the presence of one or more domains from  $\text{CaR}$  or  $\text{mGluR}$  are useful to present  $\text{GABA}_B\text{R}$  domain(s) to a binding agent in a form more like the  $\text{GABA}_B\text{R}$  domain(s) in the wild type receptor compared to an incomplete  $\text{GABA}_B\text{R}$  receptor fragment lacking one or more domains.

30 Binding assays can be carried out using techniques well known in the art. Binding assays preferably employ radiolabeled binding agents.

An example of a binding procedure is carried out by first attaching chimeric  $\text{GABA}_B\text{R}$  to a solid-phase support to create an  
35 affinity matrix. The affinity matrix is then contacted with

potential GABA<sub>A</sub>R binding agents. A large library of compounds may be used to determine those compounds binding to the affinity matrix. Bound compounds can be eluted from the column.

5

#### Therapeutic Modulation

As pointed out above, different types of diseases and disorders can be treated using compounds modulating CaR, mGluR, or GABA<sub>A</sub>R activity. Additionally, such compounds can be used prophylactically. Compounds modulating GABA<sub>A</sub>R2 activity can be administered to patients who would benefit from such treatment. Patients are mammals, preferably humans.

Modulators of CaR, mGluR, or GABA<sub>A</sub>R activity can be administered to a patient using standard techniques. Techniques and formulations generally may be found in Remington's  
15 Pharmaceutical Sciences, 18<sup>th</sup> ed., Mack Publishing Co., Easton, PA, 1990 (hereby incorporated by reference herein).

Suitable dosage forms, in part, depend upon the use or the route of entry, for example, oral, transdermal, transmucosal, or by injection (parenteral). Such dosage forms should allow the therapeutic agent to reach a target cell whether the target cell is present in a multicellular host or in culture. For example, pharmacological compounds or compositions injected into the blood stream should be soluble. Other factors are well known in the art, and include considerations such as toxicity and dosage forms which retard the therapeutic agent from exerting its effect.

Therapeutic compounds can be formulated as pharmaceutically acceptable salts and complexes thereof. Pharmaceutically acceptable salts are non-toxic salts in the amounts and concentrations at which they are administered. The preparation of such salts can facilitate the pharmacological use by altering the physical characteristics of the compound without preventing it from exerting its physiological effect. Useful alterations in physical properties include lowering the melting point to facilitate transmucosal administration and increasing the

solubility to facilitate administering higher concentrations of the drug.

The pharmaceutically acceptable salt of a compound may be present as a complex. Examples of complexes include an 8-chlorotheophylline complex (analogous to, e.g.,  
5 dimenhydrinate:diphenhydramine 8-chlorotheophylline (1:1) complex; Dramamine) and various cyclodextrin inclusion complexes.

Pharmaceutically acceptable salts include acid addition salts such as those containing sulfate, hydrochloride, fumarate,  
10 maleate, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, cyclohexylsulfamate and quinate.

Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, maleic acid, sulfuric acid, phosphoric  
15 acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, cyclohexylsulfamic acid, fumaric acid, and quinic acid.

Pharmaceutically acceptable salts also include basic  
20 addition salts such as those containing benzathine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine, procaine, aluminum, calcium, lithium, magnesium, potassium, sodium, ammonium, alkylamine, and zinc, when acidic functional groups, such as carboxylic acid or phenol are present.  
25 For example, see Remington's Pharmaceutical Sciences, 18<sup>th</sup> ed., Mack Publishing Co., Easton, PA, p. 1445, 1990. Such salts can be prepared using the appropriate corresponding bases.

Carriers or excipients can also be used to facilitate administration of therapeutic agents. Examples of carriers  
30 include calcium carbonate, calcium phosphate, various sugars such as lactose, glucose, or sucrose, or types of starch, cellulose derivatives, gelatin, vegetable oils, polyethylene glycols and physiologically compatible solvents. Examples of physiologically compatible solvents include sterile solutions of water for  
35 injection (WFI), saline solution and dextrose.

GABA<sub>B</sub>R modulating compounds can be administered by different routes including intravenous, intraperitoneal, subcutaneous, intramuscular, oral, topical (transdermal), or transmucosal administration. For systemic administration, oral administration  
5 is preferred. For oral administration, for example, the compounds can be formulated into conventional oral dosage forms such as capsules, tablets, and liquid preparations such as syrups, elixirs, and concentrated drops.

Alternatively, injection (parenteral administration) may be  
10 used, e.g., intramuscular, intravenous, intraperitoneal, and subcutaneous. For injection, compounds are formulated in liquid solutions, preferably, in physiologically compatible buffers or solutions, such as saline solution, Hank's solution, or Ringer's solution. In addition, the compounds may be formulated in solid  
15 form and redissolved or suspended immediately prior to use. Lyophilized forms can also be produced.

Systemic administration can be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be  
20 permeated are used in the formulation. Such penetrants are well known in the art, and include, for example, for transmucosal administration, bile salts and fusidic acid derivatives. In addition, detergents may be used to facilitate permeation. Transmucosal administration, for example, may be through nasal  
25 sprays, rectal suppositories, or vaginal suppositories.

For topical administration, compounds can be formulated into ointments, salves, gels, or creams, as is well known in the art.

The amounts of various GABA<sub>B</sub>R modulating compounds to be administered can be determined by standard procedures taking into  
30 account factors such as the compound IC<sub>50</sub>, EC<sub>50</sub>, the biological half-life of the compound, the age, size and weight of the patient, and the disease or disorder associated with the patient. The importance of these and other factors to be considered are well known to those of ordinary skill in the art. Generally, the

amount is expected to preferably be between about 0.01 and 50 mg/kg of the animal to be treated.

#### EXAMPLES

5           Examples are provided below illustrating different aspects and embodiments of the present invention. The examples include techniques that can be used to produce and use G-protein fusion receptors and chimeric receptors. These examples are not intended to limit the claimed invention.

10

#### Example 1: Construction of G-Protein Fusions

          This example illustrates different G-protein fusion receptor constructs and techniques used to produce different G-protein fusion receptor constructs. Numbering of nucleotide position for  
15 all the following constructs is such that nucleotide number 1 corresponds to the A of the ATG start codon of the nucleotide sequence encoding the designated protein.

#### I. FULL-LENGTH CONSTRUCTS

##### 20   A. phCaR

          The cDNA encoding the human CaR (Garrett et al., (1995) J. Biol. Chem. 270:12919) is harbored in the Bluescript SK(-) plasmid (Stratagene). This construct is referred to as phCaR.

##### 25   B. phmGluR2

          A full length human mGluR2 cDNA was amplified from human cerebellum MarathonReady cDNA (Clontech) using PCR primers based on the human mGluR2 cDNA sequence (Genbank Accession # 4504136). The obtained PCR fragment was subcloned into the pT7Blue TA  
30 vector (Novagen). A Hind III-Not I fragment containing the human mGluR2 cDNA was then subcloned into the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phmGluR2.

##### C. phGα<sub>q</sub>

35           A full length human Gα<sub>q</sub> cDNA was amplified from human cerebral cortex Quick-Clone cDNA (Clontech) using PCR primers based on the human Gα<sub>q</sub> cDNA sequence (Genbank Accession # 4504044). The obtained PCR fragment was subcloned into the



Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phG $\alpha_q$ .

D. phmGluR8

5       The cDNA encoding the full length human mGluR8 cDNA (Stormann et al., International Publication No. WO97/48724) is harbored in the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as phmGluR8.

10                   II. G $\alpha_q$ i5

      The cDNA encoding the human G $\alpha_q$ i5 cDNA (Conklin et al (1993) Nature 363:274-77) is harbored in the Bluescript SKII(-) plasmid (Stratagene). This construct is referred to as G $\alpha_q$ i5. The nucleic acid and amino acid sequences for G $\alpha_q$ i5 are provided by  
15   SEQ. ID. NOS. 28 and 29 respectively.

III. phCaR/hmGluR2

      This chimera contains the extracellular domain of the human CaR and transmembrane domain and intracellular cytoplasmic tail  
20   of human mGluR2. The chimeric junction between the CaR and hmGluR2 was created using a recombinant PCR strategy similar to those described above.

      The first reaction used two primers, CA1156 (sense 19-mer, corresponding to nucleotides 1156-1174 of human CaR), and the  
25   hybrid primer CA/2 (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 1774-1794 of human CaR and 21 nucleotides complementary to nucleotides 1660-1680 of the human mGluR2). These primers were used to amplify a 659 bp PCR fragment of human CaR.

30       In a separate PCR reaction using phmGluR2 as template, a 692 bp fragment of the human mGluR2 was amplified using a hybrid primer 2/CA (sense 42-mer, exactly complementary to primer CA/2) and oligo 2-2330m, (antisense 23-mer, complementary to nucleotides 2309-2331 of the human mGluR2 cDNA). The two PCR  
35   products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CA1156 and 2-2330m, and the Pfu DNA polymerase (Stratagene).

The resulting chimeric PCR product was digested with SexA1 (Boehringer Mannheim) and BamHI (New England Biolabs) and subcloned into phCaR digested with the same two restriction enzymes. In the final cloning step, the 3' end of human mGluR2 was subcloned into this construct using the restriction enzymes BsrGI and BamHI (both New England Biolabs). The sequence of the resultant chimeric construct, phCaR/hmGluR2, was verified by ABI automated DNA sequence analysis.

#### 10 IV. phCaR/hmGluR2\*Gqi5

This construct contains the phCaR/hmGluR2 chimeric receptor fused to human G $\alpha$ <sub>qi5</sub>. A HindIII-BamHI fragment containing the phCaR/hmGluR2 construct was subcloned into pcDNA3.1/Hygro(+) (Invitrogen) to aid in constructing this fusion protein. The chimeric junction between the C-terminus of phCaR/hmGluR2 and the N-terminus of G $\alpha$ <sub>qi5</sub> was created using a recombinant PCR strategy similar to those described above.

The first reaction used two primers, 2-1713 (sense 21-mer, corresponding to nucleotides 1710-1730 of human mGluR2) and the hybrid primer 2/Q (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 2596-2616 of human mGluR2, and 21 nucleotides complementary to nucleotides 1-21 of pG $\alpha$ <sub>qi5</sub>). These primers were used to amplify a 927 bp PCR fragment of phCaR/hmGluR2. In a separate PCR reaction all of G $\alpha$ <sub>qi5</sub> was amplified using a hybrid primer Q/2 (sense 42-mer, exactly complementary to primer 2/Q) and the and the T3 primer commercially available from Stratagene.

These two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers 2-1713 and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with Bsu361 and BamHI (New England Biolabs) and subcloned into phCaR/hmGluR2 digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, phCaR/hmGluR2\*G $\alpha$ <sub>qi5</sub>, was verified by DNA sequence analysis.

V. phmGluR2//CaR Construct

This chimera contains the extracellular and transmembrane domains of human mGluR2 linked to the intracellular cytoplasmic tail domain of the human CaR. The chimeric junction was created  
5 using three separate PCR reactions.

The first reaction used two primers, 2-1713 (sense 21-mer, corresponding to nucleotides 1710-1730 of human mGluR2, Genbank Accession # 4504136) and the hybrid primer 2/CT (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 2452  
10 - 2472 of human mGluR2 and 21 nucleotides complementary to nucleotides 2602-2622 of the human CaR). These primers were used to amplify a 783 bp PCR fragment of human mGluR2. In a separate PCR reaction using phCaR in the BlueScript SK<sup>-</sup> plasmid as  
15 template, a 750 bp fragment of the human CaR was amplified using a hybrid primer CT/2 (sense 42-mer, exactly complementary to primer 2/CT) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the  
20 external primers 2-1713 and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BsrG I and Not I (New England Biolabs) and subcloned into pmGluR2 digested with the same two restriction enzymes. The sequence of the resultant chimeric construct, pmGluR2//CaR, was  
25 verified by ABI automated DNA sequence analysis.

VI. pmGluR2//CaR\*G $\alpha$ q15 Construct

This construct contains the hmGluR2//CaR chimeric receptor fused to human G $\alpha$ q15. The chimeric junction between the C-  
30 terminus of hmGluR2//CaR and the N-terminus of G $\alpha$ q15 was created using a recombinant PCR strategy similar to that described above for the construction of phmGluR2//CaR.

The first reaction used two primers, CRP10A (sense 18-mer, corresponding to nucleotides 2812-2829 of phCaR) and the hybrid  
35 primer CaRQ (antisense 42-mer, containing 21 nucleotides complementary to nucleotides 3214- 3234 phCaR, and 21 nucleotides complementary to nucleotides 1-21 of pG $\alpha$ q15). These primers were used to amplify a 443 bp PCR fragment of hmGluR2//CaR. In a

separate PCR reaction, all of  $G\alpha_{q15}$  was amplified using a hybrid primer QCaR (sense 42-mer, exactly complementary to primer CaRQ) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CRP10A and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BstE II and Not I (New England Biolabs) and subcloned into pmGluR2//CaR digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, pmGluR2//CaR\* $G\alpha_{q15}$ , was verified by ABI automated DNA sequence analysis.

#### VII. Fusion Receptor Protein Linker Addition Constructs

##### A. phmGluR2//CaR\*AAA\* $G\alpha_{q15}$

A linker encoding three alanine residues was incorporated into the phmGluR2//CaR\* $G\alpha_{q15}$  construct by mutagenesis (Stratagene QuickChange Mutagenesis Kit). A sense 40-mer, 2CQ+LP, contained 16 nucleotides corresponding to 3219-3234 of human CaR, followed by the 9 nucleotide sequence (GCGGCCGCC) encoding three alanine residues and a NotI restriction enzyme site, and then 15 nucleotides corresponding to nucleotides 1-15 of  $G\alpha_{q15}$ . 2CQ+LP was annealed to an antisense 40-mer, 2CQ+LM, the exact complement of 2CQ+LP. These oligos were used in the mutagenesis reaction according to the manufacturer's protocol. Restriction enzyme analysis and DNA sequence analysis confirmed the insertion of the 9 nucleotide linker (GCGGCCGCC) between the C-terminus of phmGluR2//CaR and the N-terminus of  $G\alpha_{q15}$ . This construct was designated phmGluR2//CaR\*AAA\* $G\alpha_{q15}$ .

##### B. Human GABA<sub>B</sub>R2\*AAA\* $G\alpha_{qo5}$ and human GABA<sub>B</sub>R1a\*AAA\* $G\alpha_{qo5}$

These constructs contain the human GABA<sub>B</sub>R2 (hGABA<sub>B</sub>R2: Genbank Accession # AJ 012188) and human GABA<sub>B</sub>R1a (hGABA<sub>B</sub>R1a: Genbank Accession # AJ 012185) fused at their C-terminus to the N-terminus of human  $G\alpha_{qo5}$  (h $G\alpha_{qo5}$ : Nature 363:274-276, 1993). Human GABA<sub>B</sub>R2, hGABA<sub>B</sub>R1a, and h $G\alpha_{qo5}$  were cloned into the plasmid pcDNA3.1/Hygro+ (Invitrogen) and are designated phGABA<sub>B</sub>R2,

phGABA<sub>B</sub>R1a, and phGα<sub>o</sub>5. The first reaction used two primers, XcmI-R2 (sense 20-mer, corresponding to nucleotides 2650-2669 of phGABA<sub>B</sub>R2) and the hybrid primer R2/Go5(-) (antisense 45-mer, containing 18 nucleotides complementary to nucleotides 2806-2823 of phGABA<sub>B</sub>R2 and 18 nucleotides complementary to nucleotides 1-18 of hGα<sub>o</sub>5). These two complementary areas flank a 9 nucleotide sequence coding for 3 alanine sequences with a unique NotI restriction site. These primers were used to amplify a 200 base-pair PCR fragment.

In a separate PCR reaction, part of hGα<sub>o</sub>5 was amplified using a hybrid primer R2/Gα<sub>o</sub>5(+) (sense 45-mer), exactly complementary to R2/Go5(-) and XbaI-Go5 primer (22-mer containing 22 nucleotides complementary to nucleotides 873-895 of hGα<sub>o</sub>5). These primers were used to amplify a 914 base-pair PCR product. The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers; XcmI-R2 and XbaI-Go5, and Pfu polymerase (Stratagene).

The resulting chimeric PCR product was digested with the restriction endonucleases XcmI and XbaI (New England Biolabs) and subcloned into phGABA<sub>B</sub>R2 digested with the same two restriction enzymes. The resulting clone was then digested with HindIII and XbaI and subcloned into phGα<sub>o</sub>5 cut with HindIII and XbaI resulting in the chimeric hGABA<sub>B</sub>R\*AAA\*Gα<sub>o</sub>5. The chimeric junction between the C-terminus hGABA<sub>B</sub>R1a, the Ala linker, and the N-terminus of hGα<sub>o</sub>5 was created using a recombinant PCR strategy similar to those described above.

To construct hGABA<sub>B</sub>R1a\*AAA\*Gqo5, the first reaction used a commercially available T7 primer (Novagen) and the NtI hGBR1 primer (CAGAGTCATGGCGGCCGCCTTATAAAGCAAATGCACTCG) corresponding to nucleotide numbers 1-9 of hGα<sub>o</sub>5 and nucleotide numbers 2863-2883 of hGABA<sub>B</sub>R1a.

#### VIII. phmGluR8//CaR Construct

This chimera contains the extracellular and transmembrane domains of human mGluR8 linked to the intracellular cytoplasmic tail domain of the human CaR. The chimeric junction between hmGluR8 and the CaR was created using a recombinant PCR strategy

similar to those described above.

The first reaction used two primers, CH5A (sense 19-mer, corresponding to nucleotides 2187-2205 of human mGluR8, Stormann et al., International Publication Number WO97/48724) and the hybrid primer CH5B (antisense 40-mer, containing 22 nucleotides complementary to nucleotides 2523 - 2544 of human mGluR8, and 18 nucleotides complementary to nucleotides 2602-2619 of the human CaR). These primers were used to amplify a 375 bp PCR fragment of human mGluR8. In a separate PCR reaction using phCaR in the BlueScript SK(-) plasmid as template, a 750 bp fragment of the human CaR was amplified using a hybrid primer CH5C (sense 40-mer, exactly complementary to primer CH5B) and the T3 primer commercially available from Stratagene.

The two PCR products generated from the above two reactions were annealed together in equimolar ratios in the presence of the external primers CH5A and T3, and the Pfu DNA polymerase (Stratagene). The resulting chimeric PCR product was digested with BsrG I and Xba I (New England Biolabs) and subcloned into pmGluR8 digested with the same two restriction enzymes. The sequence of the resultant chimeric construct, pmGluR8//CaR, was verified by DNA sequence analysis.

#### IX. mGluR8//CaR\*G $\alpha$ q15 Construct

This construct contains the hmGluR8//CaR chimeric receptor fused to human G $\alpha$ q15. The chimeric junction between the C-terminus of hmGluR8//CaR and the N-terminus of G $\alpha$ q15 was created using a recombinant PCR strategy similar to that described above for the construction of phmGluR2//CaR\*G $\alpha$ q15.

The first reaction used two primers, CRP10A (sense 18-mer, corresponding to nucleotides 2812-2829 of phCaR) and the hybrid primer Gqi5/CaR (antisense 40-mer, containing 21 nucleotides complementary to nucleotides 3214-3234 phCaR, and 19 nucleotides complementary to nucleotides 1-19 of pG $\alpha$ q15). These primers were used to amplify a 441 bp PCR fragment of hmGluR8//CaR.

In a separate PCR reaction all of G $\alpha$ q15 was amplified using a hybrid primer CaR/Gqi5 (sense 40-mer, exactly complementary to primer Gqi5/CaR) and the Apa I-mut primer (20-mer). The two PCR products generated from the above two reactions were annealed

together in equimolar ratios in the presence of the external primers CRP10A and Apa I-mut, and the Pfu DNA polymerase (Stratagene).

The resulting chimeric PCR product was digested with BstE II and Apa I (New England Biolabs) and subcloned into pmGluR8//CaR digested with the same two restriction enzymes. The sequence of the resultant chimeric fusion construct, pmGluR8//CaR\*G $\alpha$ q15, was verified by DNA sequence analysis.

10 Example 2: Functional Expression of CaR/GABA $_A$ R2

In vitro transcribed RNA (7 ng) encoding a chimeric CaR/GABA $_A$ R2 (CaR extracellular and transmembrane domains, and intracellular GABA $_A$ R2 domain) was co-injected with in vitro transcribed RNA (2 ng) encoding G $\alpha$ 15 into *Xenopus* oocytes. Following a 72-hour incubation, the oocytes were voltage-clamped using standard electrophysiological techniques (Hille, B., Ionic Channels of Excitable Membranes, pp.30-33, Sinauer Associates, Inc., Sunderland, Ma., 1992). Activation of the chimeric receptor was detected by increases in the calcium-activated chloride current.

Application of the CaR activator 100  $\mu$ M Gd $^{3+}$ , resulted in reversible, oscillatory increases in the calcium-activated chloride current as shown in Figure 8. These data demonstrate the functional response of the chimeric CaR/GABA $_A$ R2 receptor upon activation via a site within the CaR extracellular domain. In this assay, the G $\alpha$ 15 subunit acts to promote signal transduction through intracellular pathways that mobilize intracellular Ca $^{2+}$ .

Example 3: Expression of Different G-Protein Fusion Receptors

30 The ability of different G-protein fusions to transduce signal resulting from ligand binding is shown in Figure 15. The different G-protein fusion receptors used in this example were as follows: mGluR2//CaR\*Gqi5 (SEQ. ID. NO. 37), CaR/mGluR2\*Gqi5 (SEQ. ID. NO. 33), and mGluR8//CaR\*Gqi5 SEQ. ID. NO. 41.

35 Oocytes suitable for injection were obtained from adult female *Xenopus laevis* toads using procedures described in C. J.

Marcus-Sekura and M. J. M. Hitchcock, Methods in Enzymology, Vol. 152 (1987).

Receptor fusion cRNAs were dissolved in water and 50 nl (12.5 ng/oocyte) were injected into individual oocytes.

5 Following injection, oocytes were incubated at 16°C in MBS containing 1 mM CaCl<sub>2</sub> for 2 to 7 days prior to electrophysiological recording.

Test substances were applied by superfusion at a flow rate of about 5 ml/min. Receptor fusion activation was determined by  
10 measuring the increase in calcium-activated chloride current (I<sub>Cl</sub>). Increases in I<sub>Cl</sub> were quantified by measuring the peak inward current stimulated by activating agent, relative to the holding current at -60 mV. Application of 100 μM L-glutamate elicited a response from the mGluR2//CaR\*Gαq15 and  
15 mGluR8//CaR\*Gαq15. Application of 100 μM Gd<sup>3+</sup> activated the CaR/mGluR2\*Gq15.

Other embodiments are within the following claims. Thus, while several embodiments have been shown and described, various  
20 modifications may be made, without departing from the spirit and scope of the present invention.



Claims

1. A G-protein fusion receptor comprising  
an extracellular domain comprising an extracellular domain  
5 amino acid sequence substantially similar to either an  
extracellular CaR amino acid sequence, an extracellular mGluR  
amino acid sequence, or an extracellular GABA<sub>B</sub> receptor amino acid  
sequence;  
a transmembrane domain joined to the carboxy terminus of  
10 said extracellular domain, said transmembrane domain comprising a  
transmembrane domain amino acid sequence substantially similar to  
either a transmembrane CaR amino acid sequence, a transmembrane  
mGluR amino acid sequence, or a transmembrane GABA<sub>B</sub> receptor amino  
acid sequence;  
15 an intracellular domain joined to the carboxy terminus of  
said transmembrane domain comprising all or a portion of an  
intracellular amino acid sequence substantially similar to either  
an intracellular CaR amino acid sequence, an intracellular mGluR  
amino acid sequence, or an intracellular GABA<sub>B</sub> receptor amino acid  
20 sequence, provided that said portion is at least about 10 amino  
acids;  
an optionally present linker joined to the carboxy terminus  
of said intracellular domain; and  
a G-protein joined either to said intracellular domain or to  
25 said optionally present linker, provided that said G-protein is  
joined to said optionally present linker when said optionally  
present linker is present.
2. The G-protein fusion receptor of claim 1, wherein said  
30 extracellular domain consists of said extracellular domain amino  
acid sequence, said transmembrane domain consists of said  
transmembrane domain amino acid sequence; and said intracellular  
domain consists of said transmembrane domain amino acid sequence.
- 35 3. The G-protein fusion receptor of claim 2, wherein said  
optionally present linker is present and is a polypeptide 3 to 30  
amino acids in length.

4. The G-prot in fusion receptor of claim 2, wherein said optionally present linker is not present.

5. The G-protein fusion receptor of claim 3 or 4, wherein  
5 said G-protein is selected from the group consisting of:  $G_{\alpha 15}$ ,  
 $G_{\alpha 16}$ , Gqo5, and Gqi5

6. The G-protein fusion of claim 5, wherein any of said  
CaR sequence present is a human CaR sequence, any of said mGluR  
10 sequence present is from a human mGluR, and any of said GABA<sub>B</sub>  
receptor sequence present is from human mGluR.

7. A nucleic acid comprising a nucleotide sequence  
encoding for the G-protein fusion of any one of claims 1-6.  
15

8. An expression vector comprising a nucleotide sequence  
encoding for the G-protein fusion of any one of claims 1-6  
transcriptionally coupled to a promoter.

9. A recombinant cell comprising the expression vector of  
20 claim 8 and a cell wherein the G-protein fusion is expressed and  
is functional.

10. A recombinant cell produced by combining a vector  
25 comprising the nucleic acid of claim 9 and elements for  
introducing heterologous nucleic acid into a cell wherein the G-  
protein fusion receptor is expressed, and said cell.

11. A process for the production of a G-protein fusion  
30 receptor comprising:  
growing procaryotic or eukaryotic host cells comprising a  
nucleic acid sequence expressing the G-protein fusion receptor of  
any one of claims 1-6, under suitable nutrient conditions  
allowing for cell growth.

35  
12. A method of measuring the ability of a compound to  
effect G-protein fusion activity comprising the steps of:

a) providing said compound to a cell expressing the G-  
protein fusion receptor of any one of claims 1-6, and

b) measuring the ability of said compound to affect the activity of said receptor as an indication of the ability of said compound to effect G-protein fusion receptor activity.

- 5           13. A chimeric receptor comprising  
          an extracellular domain comprising an extracellular domain  
          amino acid sequence substantially similar to a sequence selected  
          from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID  
          NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5;  
10           a transmembrane domain comprising a transmembrane domain  
          amino acid sequence substantially similar to a sequence selected  
          from the group consisting of SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID  
          NO: 8, SEQ ID NO: 9, and SEQ ID NO: 10; and  
          an intracellular cytoplasmic domain comprising an  
15           intracellular domain amino acid sequence substantially similar to  
          a sequence selected from the group consisting of SEQ ID NO: 11,  
          SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14;  
          wherein at least one domain is present which comprises an  
          amino acid sequence substantially similar to a sequence selected  
20           from the group consisting of: SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID  
          NO: 4, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, SEQ ID NO:  
          12, SEQ ID NO: 13, and SEQ ID NO: 14; and at least one domain is  
          present which comprises an amino acid sequence substantially  
          similar to a sequence selected from the group consisting of: SEQ  
25           ID NO: 1, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 10, SEQ ID NO:  
          11, and SEQ ID NO: 15.

14. The chimeric receptor of claim 13 wherein said  
          extracellular domain has a sequence similarity of at least 90%  
30           with an amino acid sequence selected from the group consisting of  
          SEQ ID NOs: 2, 3, and 4; said transmembrane domain has a sequence  
          similarity of at least 90% with an amino acid sequence selected  
          from the group consisting of SEQ ID Nos: 6, 7, 8, 9, and 10; and  
          said intracellular domain has a sequence similarity of at least  
35           90% with an amino acid sequence selected from the group  
          consisting of SEQ ID NOs: 11 and 15.

15. The chimeric receptor of claim 14, wherein said  
          extracellular domain has a sequence similarity of at least 90%

with the amino acid sequence of SEQ ID NO: 2; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 11.

16. The chimeric receptor of claim 14, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 3; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

17. The chimeric receptor of claim 14, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence SEQ ID NO: 4; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

18. The chimeric receptor of claim 13, wherein said extracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4 and 5; said transmembrane domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID Nos: 7, 8, and 9; and said intracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 11, 12, 13, 14, and 15.

19. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 11.

20. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

21. The chimeric receptor of claim 18, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO 11.

22. The chimeric receptor of claim 13, wherein said extracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, and 5; said transmembrane domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID Nos: 6, 7, 8, 9, and 10; and said intracellular domain has a sequence similarity of at least 90% with an amino acid sequence selected from the group consisting of SEQ ID NOS: 12, 13, and 14.

23. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 12.

24. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino

acid sequence of SEQ ID NO: 7; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 12.

5           25. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 8; and said intracellular domain has  
10 a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 13.

          26. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90%  
15 with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid  
20 sequence of SEQ ID NO: 13.

          27. The chimeric receptor of claim 22, wherein said extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino  
25 acid sequence of SEQ ID NO: 9; and said intracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 14.

          28. The chimeric receptor of claim 22, wherein said  
30 extracellular domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 1; said transmembrane domain has a sequence similarity of at least 90% with the amino acid sequence of SEQ ID NO: 6; and said intracellular domain has a sequence similarity of at least 90% with the amino acid  
35 sequence of SEQ ID NO: 14.

          29. The chimeric receptor of any one of claims 13-28, wherein said receptor functional couples to a G-protein.

30. The chimeric receptor of any one of claims 13-28, wherein said chimeric receptor consists of said extracellular domain, said transmembrane domain, said intracellular domain, and an optionally present G-protein  $\alpha$  subunit covalently joined to said intracellular domain.

31. The chimeric receptor of claim 30, wherein said chimeric receptor consists of said extracellular domain, said transmembrane domain, and said intracellular domain.

32. The chimeric receptor of claim 30, wherein said G-protein  $\alpha$  subunit consists of the amino acid sequence of SEQ ID Nos: 16 or 17.

33. A nucleic acid comprising a nucleotide sequence encoding for the chimeric receptor of any one of claims 13-32.

34. An expression vector comprising a nucleotide sequence encoding for the chimeric receptor of any one of claims 13-32 transcriptionally coupled to a promoter.

35. A recombinant cell comprising the expression vector of claim 34 and a cell wherein the chimeric receptor is expressed and is functional.

36. A recombinant cell produced by combining a vector comprising the nucleic acid of claim 33 and elements for introducing heterologous nucleic acid into a cell wherein the chimeric receptor is expressed, and said cell.

37. A process for the production of a chimeric receptor comprising:  
growing procaryotic or eukaryotic host cells comprising a nucleic acid sequence expressing the chimeric receptor of any one of claims 13-32, under suitable nutrient conditions allowing for cell growth.

38. A method of measuring the ability of a compound to effect GABA<sub>A</sub>R or mGluR activity comprising the steps of:

a) providing said compound to a cell expressing the chimeric receptor of any one of claims 13-32, and

b) measuring the ability of said compound to affect the activity of said receptor as an indication of the ability of said compound to effect GABA<sub>A</sub>R or mGluR activity.

39. The method of claim 38, wherein said method measures activity at a GABA<sub>A</sub>R.

40. The method of claim 38, wherein said method measures activity at a mGluR.

41. A fusion receptor polypeptide comprising a receptor and a G-protein  $\alpha$  subunit, wherein said G-protein  $\alpha$  subunit is fused to the intracellular domain of said receptor, provided that said receptor is not an adrenoceptor.



I/III

## ClustalW Formatted Alignments

```

SEQ ID 1 M A F Y S C C W V L L A L T W H T S A Y G P D Q R
SEQ ID 2 M L L L L L L A P L F L R P P G A G G A Q T P N A
SEQ ID 3 M G P G A P F A R V G W P L P L L V V M A A G V A
SEQ ID 4 M A S P R S S G Q P G P X P P P P P P A R L L L
SEQ ID 5 M V C E G K R S A S C P C F F L L T A K F Y W I L

```

```

SEQ ID 1 A Q K K G D I I L G G L F P I H F G V A A K D Q D
SEQ ID 2 T S E G C Q I I H P P W E G G I R Y R G L T R D Q
SEQ ID 3 P V W A S H S P H L P R P H S R V P P H P S S E R
SEQ ID 4 L L L L P L L L P L A P G A W G W A R G A P R P P
SEQ ID 5 T M M Q R T H S Q E Y A H S I R V D G D I I L G G

```

```

SEQ ID 1 L K S R P E S V E C I R Y N F R G F R W L Q A M I
SEQ ID 2 V K A I N F L P V D Y E I E Y V C R G E R E V V G
SEQ ID 3 R A V Y I G A L F P M S G G W P G G Q A C Q P A V
SEQ ID 4 P S S P P L S I M G L M P L T K E V A K G S I G R
SEQ ID 5 L F P V H A K G E R G V P C G E L K K E K G I H R

```

```

SEQ ID 1 F A I E E I N S S P A L L P N L T L G Y R I F D T
SEQ ID 2 P K V R K C L A N G S W T D M D T P S R C V R I C
SEQ ID 3 E M A L E D V N S R R D I L P D Y E L K L I H H D
SEQ ID 4 G V L P A V E L A I E Q I R N E S L L R P Y F L D
SEQ ID 5 L E A M L Y A I D Q I N K D P D L L S N I T L G V

```

```

SEQ ID 1 C N T V S K A L E A T L S F V A Q N K I D S L N L
SEQ ID 2 S K S Y L T L E N G K V F L T G G D L P A L D G A
SEQ ID 3 S K C D P G Q A T K Y L Y E L L Y N D P I K I I L
SEQ ID 4 L R L Y D T E C D N A K G L K A F Y D A I K Y G P
SEQ ID 5 R I L D T C S R D T Y A L E Q S L T F V Q A L I E

```

```

SEQ ID 1 D E F C N C S E H I P S T I A V V G A T G S G V S
SEQ ID 2 R V D F R C D P D F H L V G S S R S I C S Q G Q W
SEQ ID 3 M P G C S S V S T L V A E A A R M W N L I V L S Y
SEQ ID 4 N H L M V F G G V C P S V T S I I A E S L Q G W N
SEQ ID 5 K D A S D V K C A N G D P P I F T K P D K I S G V

```

```

SEQ ID 1 T A V A N L L G L F Y I P Q V S Y A S S S R L L S
SEQ ID 2 S T P K P H C Q V N R T P H S E R R A V Y I G A L
SEQ ID 3 G S S S P A L S N R Q R F P T F F R T H P S A T L
SEQ ID 4 L V Q L S F A A T T P V L A D K K K Y P Y F F R T
SEQ ID 5 I G A A A S S V S I M V A N I L R L F K I P Q I S

```

FIG. 1a.

2/111

SEQ ID 1 NKNQFKSFLRTIPNDEHQATAMADI  
 SEQ ID 2 FPMSSGGWPGGQACQPAVEMALEDVN  
 SEQ ID 3 HNPTRVKLF EKWGWKKIATIQQTTE  
 SEQ ID 4 VPSDNAVNPAILKLLKHYQWKR VGT  
 SEQ ID 5 YASTAPELSDNTRYDFFSRVVPDS

SEQ ID 1 IEYFRWNWVG TIAADDDYGRPGIEK  
 SEQ ID 2 SRRDILPDYELKLIHHDSKCDPGQA  
 SEQ ID 3 VFTSTLDDLEERVKEAGIEITFRQS  
 SEQ ID 4 LTQDVQRFSEVRNDLTGVLYGEDIE  
 SEQ ID 5 YQAQAMVDIVTALGWNYVSTLASEG

SEQ ID 1 FREEAEERD ICIDFSELISQYSD EE  
 SEQ ID 2 TKYLYELLYNDPIKILMPGCCSSVS  
 SEQ ID 3 FFS DPAVPVKNLKRQDARIIVGLFY  
 SEQ ID 4 ISDTESFSNDPCTSVKKLKGNDVRI  
 SEQ ID 5 NYGESGVEAFTQISREIGGVCI AQ S

SEQ ID 1 EIQHVVEVIQNSTAKVIVVFSSGPD  
 SEQ ID 2 TLVAEAAARMWN LIVLSYGSSSPALS  
 SEQ ID 3 ETEARKVFCEVYKERLFGKKYVWFL  
 SEQ ID 4 ILGQFDQNMAAKVFCCAYEENMYGS  
 SEQ ID 5 QKIPREPRPGEF EKIIKRLLLETPNA

SEQ ID 1 LEPLIKEIVRRNITGKIWLASEAWA  
 SEQ ID 2 NRQRFPTFFRTHPSATLHNPTRVKL  
 SEQ ID 3 IGWYADNWFKIYDPSINCTVDEMTE  
 SEQ ID 4 KYQWIIPGWYEPSWWEQVHTEANSS  
 SEQ ID 5 RAVIMFANEDDIRRILEAAKKLNQS

SEQ ID 1 SSSLIAMPPQYFHVVG GTIGFALKAG  
 SEQ ID 2 FEKWWGKKIATIQQTTEVFTSTLDD  
 SEQ ID 3 AVEGHITTEIVMLNPANTRSI SNMT  
 SEQ ID 4 RCLRKNNLLAAMEGYIGVDFEPLSSK  
 SEQ ID 5 GHFLWIGSDSWGSKIAPVYQQEEIA

SEQ ID 1 QIPGFREFLKKVHPRKSVHNGFAKE  
 SEQ ID 2 LEERVKEAGIEITFRQSFFSDPAVP  
 SEQ ID 3 SQEFVEKLTKR LKRHP EETGGFQEA  
 SEQ ID 4 QIKTISGKTPQQYEREYNNKRSGVG  
 SEQ ID 5 EGAVTILPKRASIDGFDRYFRSRTL

FIG. 1b.

3/III

SEQ ID 1 FWEETFNCHLQEGAKGPLPVDTF LR  
 SEQ ID 2 VKNLKRQDARIIVGLFYETEARKVF  
 SEQ ID 3 PLAYDAIWALALALNKTSGGGGRSG  
 SEQ ID 4 PSKFHGYAYDGIWVIAKT LQRAMET  
 SEQ ID 5 ANNRRNVWF AEFWEENFGCKLGSHG

SEQ ID 1 GHEESGDRFSNSSTA FRPLCTGDEN  
 SEQ ID 2 CEVYKERLFGKKYVWFLIGWYADNW  
 SEQ ID 3 VRLED FNYNNQTITDQIYRAMNSSS  
 SEQ ID 4 LHASSRHQRIQDFNYTDHTLGR IIL  
 SEQ ID 5 KRNSHIKKCTGLERIARDSSSYEQEG

SEQ ID 1 ISSVETPYIDYTHLRISYNVYLAVY  
 SEQ ID 2 FKIYDPSINCTVDEMTEAVEGHITT  
 SEQ ID 3 FEGVSGHVVFDA SSGSRMAWTLIEQL  
 SEQ ID 4 NAMNETNFFFGVTGQVVFRNGERMGT  
 SEQ ID 5 KVQFVIDAVYSMAYALHNMHKDLC P

SEQ ID 1 SIAHALQDIYTCLPGRGLFTNGSCA  
 SEQ ID 2 EIVMLNPANTRSISNMTS QEFVEKL  
 SEQ ID 3 QGGSYKKIGYYDSTKDDLSWSKTDK  
 SEQ ID 4 IKFTQFQDSREVKVGEYNAVADTLE  
 SEQ ID 5 GYIGLCPRMSTIDGKEL LGYIRAVN

SEQ ID 1 DIKKVEAWQVLKHLRHLNFTNNMGE  
 SEQ ID 2 TKRLKRHP EETGGFQEAPLAYDAIW  
 SEQ ID 3 WIGGSPPADQTLVIKTFRFLSQK  
 SEQ ID 4 IINDTIRFQGS EPPKDKTIILEQLR  
 SEQ ID 5 FNGSAGTPVTFNENGDA PGRYDIFQ

SEQ ID 1 QVTFDEC GDLVGNYSIINWHLSPED  
 SEQ ID 2 ALALALNKTSGGGGRSGVRLED FNY  
 SEQ ID 3  
 SEQ ID 4 KISLP  
 SEQ ID 5 YQITNKSTEYKVIGHWTNQLHLKVE

SEQ ID 1 GSIVFKEVGYYNVYAKKGERLFINE  
 SEQ ID 2 NNQTITDQIYRAMNSSS SFEGVSGHV  
 SEQ ID 3  
 SEQ ID 4  
 SEQ ID 5 DMQWAHREH THPASVCSLPCKPGER

FIG. 1c.

4/III

SEQ ID 1 E K I L W S G F S R E V P F S N C S R D C L A G T  
SEQ ID 2 V F D A S G S R M A W T L I E Q L Q G G S Y K K I  
SEQ ID 3  
SEQ ID 4  
SEQ ID 5 K K T V K G V P C C W H C E R C E G Y N Y Q V D E

SEQ ID 1 R K G I I E G E P T C C F E C V E C P D G E Y S D  
SEQ ID 2 G Y Y D S T K D D L S W S K T D K W I G G S P P A  
SEQ ID 3  
SEQ ID 4  
SEQ ID 5 L S C E L C P L D Q R P N M N R T G C Q L I P I I

SEQ ID 1 E T D A S A C N K C P D D F W S N E N H T S C I A  
SEQ ID 2 D Q T L V I K T F R F L S Q K  
SEQ ID 3  
SEQ ID 4  
SEQ ID 5 K L E W H S P W

SEQ ID 1 K E I E F L S W T E P F  
SEQ ID 2  
SEQ ID 3  
SEQ ID 4  
SEQ ID 5

*FIG. 1d.*

5/III

SEQ ID 6 G I A L T L F A V L G I F L T A F V L G V F I K F R N T P I  
 SEQ ID 7 L F I S V S V L S S L G I V L A V V C L S F N I Y N S H V R  
 SEQ ID 8 L F I S V S V L S S L G I V L A V V C L S F N I Y N S H V R  
 SEQ ID 9 L Y S I L S A L T I L G M I M A S A F L F F N I K N R N Q K  
 SEQ ID 10 A V V P V F V A I L G I I A T T F V I V T F V R Y N D T P I

SEQ ID 6 V K A T N R E L S Y L L L F S L L C C F S S S L F F I G E P  
 SEQ ID 7 Y I Q N S Q P N L N N L T A V G C S L A L A A V F P L G L D  
 SEQ ID 8 Y I Q N S Q P N L N N L T A V G C S L A L A A V F P L G L D  
 SEQ ID 9 L I K M S S P Y M N N L I I L G G M L S Y A S I F L F G L D  
 SEQ ID 10 V R A S G R E L S Y V L L T G I F L C Y S I T F L M I A A P

SEQ ID 6 Q D W T C R L R Q P A F G I S F V L C I S C I L V K T N R V  
 SEQ ID 7 G Y H I G R N Q F P F V C Q A R L W L L G L G F S L G Y G S  
 SEQ ID 8 G Y H I G R N Q F P F V C Q A R L W L L G L G F S L G Y G S  
 SEQ ID 9 G S F V S E K T F E T L C T V R T W I L T V G Y T T A F G A  
 SEQ ID 10 D T I I C S F R R V F L G L G M C F S Y A A L L T K T N R I

SEQ ID 6 L L V F E A K I P T S F H R K W W G L N L Q F L L V F L C T  
 SEQ ID 7 M F T K I W W V H T V F T K K E E K K E W R K T L E P W K L  
 SEQ ID 8 M F T K I W W V H T V F T K K E E K K E W R K T L E P W K L  
 SEQ ID 9 M F A K T W R V H A I F K N V K M K K K I I K D Q K L L V I  
 SEQ ID 10 H R I F E Q G K K S V T A P K F I S P A S Q L V I T F S L I

SEQ ID 6 F M Q I V I C V I W L Y T A P P S S Y R N Q E L E D E I I F  
 SEQ ID 7 Y A T V G L L V G M D V L T L A I W Q I V D P L H R T I E T  
 SEQ ID 8 Y A T V G L L V G M D V L T L A I W Q I V D P L H R T I E T  
 SEQ ID 9 V G G M L L I D L C I L I C W Q A V D P L R R T V E K Y S M  
 SEQ ID 10 S V Q L L G V F V W F V V D P P H I I I D Y G E Q R T L D P

SEQ ID 6 I T C H E G S L M A L G F L I G Y T C L L A A I C F F F A F  
 SEQ ID 7 F A K E E P K E D I D V S I L P Q L E H C S S R K M N T W L  
 SEQ ID 8 F A K E E P K E D I D V S I L P Q L E H C S S R K M N T W L  
 SEQ ID 9 E P D P A G R D I S I R P L L E H C E N T H M T I W L G I V  
 SEQ ID 10 E K A R G V L K C D I S D L S L I C S L G Y S I L L M V T C

SEQ ID 6 K S R K L P E N F N E A K F I T F S M L I F F I V W I S F I  
 SEQ ID 7 G I F Y G Y K G L L L L L G I F L A Y E T K S V S T E K I N  
 SEQ ID 8 G I F Y G Y K G L L L L L G I F L A Y E T K S V S T E K I N  
 SEQ ID 9 Y A Y K G L L M L F G C F L A W E T R N V S I P A L N D S K  
 SEQ ID 10 T V Y A I K T R G V P E T F N E A K P I G F T M Y T T C I I

FIG. 2a.

6/III

SEQ ID 6 P A Y A S T Y G K F V S A V E V I A I L A A S F G L L A C I  
SEQ ID 7 D H R A V G M A I Y N V A V L C L I T A P V T M I L S S Q Q  
SEQ ID 8 D H R A V G M A I Y N V A V L C L I T A P V T M I L S S Q Q  
SEQ ID 9 Y I G M S V Y N V G I M C I I G A A V S F L T R D Q P N V Q  
SEQ ID 10 W L A F I P I F F G T A Q S A E K M Y I Q T T T L T V S M S

SEQ ID 6 F F N K I Y I I L F  
SEQ ID 7 D A A F A F A S L A I V F S S Y I T L V V L F V P K M  
SEQ ID 8 D A A F A F A S L A I V F S S Y I T L V V L F V P K M  
SEQ ID 9 F C I V A L V I I F C S T I T L C L V F V P K L  
SEQ ID 10 L S A S V S L G M L Y M P K V Y I I I F

*FIG. 2b.*

7/III

SEQ ID 11 K P S R N T I E E V R C S T A A H A F K V A A R A T L R R S  
 SEQ ID 12 R R L I T R G E W Q S E A Q D T M K T G S S T N N N E E E K  
 SEQ ID 13 R R L I T R G E W Q S E A Q D T M K T G S S T N N N E E E K  
 SEQ ID 14 I T L R T N P D A A T Q N R R F Q F T Q N Q K K E D S K T S  
 SEQ ID 15 H P E Q N V Q K R K R S F K A V V T A A T M Q S K L I Q K G

SEQ ID 11 N V S R K R S S S L G G S T G S T P S S S I S S K S N S E D  
 SEQ ID 12 S R L L E K E N R E L E K I I A E K E E R V S E L R H Q L Q  
 SEQ ID 13 S R L L E K E N R E L E K I I A E K E E R V S E L R H Q L Q  
 SEQ ID 14 T S V T S V N Q A S T S R L E G L Q S E N H R L R M K I T E  
 SEQ ID 15 N D R P N G E V K S E L C E S L E T N S K S S V E F P M V K

SEQ ID 11 P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q Q Q P L T L P Q  
 SEQ ID 12 S R Q Q L R S R R H P P T P P E P S G G L P R G P P E P P D  
 SEQ ID 13 S R Q Q L R S R R H P P T P P E P S G G L P R G P P E P P D  
 SEQ ID 14 L D K D L E E V T M Q L Q D T P E K T T Y I K Q N H Y Q E L  
 SEQ ID 15 S G S T S

SEQ ID 11 Q Q R S Q Q Q P R C K Q K V I F G S G T V T F S L S F D E P  
 SEQ ID 12 R L S C D G S R V H L L Y K  
 SEQ ID 13 R L S C D G S R V H L L Y K  
 SEQ ID 14 N D I L N L G N F T E S T D G G K A I L K N H L D Q N P Q L  
 SEQ ID 15

SEQ ID 11 Q K N A M A H G N S T H Q N S L E A Q K S S D T L T R H Q P  
 SEQ ID 12  
 SEQ ID 13  
 SEQ ID 14 Q W N T T E P S R T C K D P I E D I N S P E H I Q R R L S L  
 SEQ ID 15

SEQ ID 11 L L P L Q C G E T D L D L T V Q E T G L Q G P V G G D Q R P  
 SEQ ID 12  
 SEQ ID 13  
 SEQ ID 14 Q L P I L H H A Y L P S I G G V D A S C V S P C V S P T A S  
 SEQ ID 15

SEQ ID 11 E V E D P E E L S P A L V V S S S Q S F V I S G G G S T V T  
 SEQ ID 12  
 SEQ ID 13  
 SEQ ID 14 P R H R H V P P S F R V M V S G L  
 SEQ ID 15

FIG. 3a.

8/III

SEQ ID 11 E N V V N S  
SEQ ID 12  
SEQ ID 13  
SEQ ID 14  
SEQ ID 15

*FIG. 3b.*



9/III

SEQ. ID. NO. 16 M A R S L T W G C C P W C L T E E E K T A A R I D Q E I N R  
SEQ. ID. NO. 17 M A R S L T W R C C P W C L T E D E K A A A R V D Q E I N R

SEQ. ID. NO. 16 I L L E Q K K Q E R E E L K L L L L G P G E S G K S T F I K  
SEQ. ID. NO. 17 I L L E Q K K Q D R G E L K L L L L G P G E S G K S T F I K

SEQ. ID. NO. 16 Q M R I I H G V G Y S E E D R R A F R L L I Y Q N I F V S M  
SEQ. ID. NO. 17 Q M R I I H G A G Y S E E E R K G F R P L V Y Q N I F V S M

SEQ. ID. NO. 16 Q A M I D A M D R L Q I P F S R P D S K Q H A S L V M T O D  
SEQ. ID. NO. 17 R A M I E A M E R L Q I P F S R P E S K H H A S L V M S O D

SEQ. ID. NO. 16 P Y K V S T F E K P Y A V A M Q Y L W R D A G I R A C Y E R  
SEQ. ID. NO. 17 P Y K V T T F E K R Y A A A M Q W L W R D A G I R A C Y E R

SEQ. ID. NO. 16 R R E F H L L D S A V Y Y L S H L E R I S E D S Y I P T A Q  
SEQ. ID. NO. 17 R R E F H L L D S A V Y Y L S H L E R I T E E G Y V P T A Q

SEQ. ID. NO. 16 D V L R S R M P T T G I N E Y C F S V K K T K L R I V D V G  
SEQ. ID. NO. 17 D V L R S R M P T T G I N E Y C F S V Q K T N L R I V D V G

SEQ. ID. NO. 16 G Q R S E R R K W I H C F E N V I A L I Y L A S L S E Y D O  
SEQ. ID. NO. 17 G Q K S E R K K W I H C F E N V I A L I Y L A S L S E Y D O

SEQ. ID. NO. 16 C L E E N D Q E N R M E E S L A L F S T I L E L P W F K S T  
SEQ. ID. NO. 17 C L E E N N Q E N R M K E S L A L F G T I L E L P W F K S T

SEQ. ID. NO. 16 S V I L F L N K T D I L E D K I H T S H L A T Y F P S F Q G  
SEQ. ID. NO. 17 S V I L F L N K T D I L E E K I P T S H L A T Y F P S F Q G

SEQ. ID. NO. 16 P R R D A E A A K S F I L D M Y A R V Y A S C A E P Q D G G  
SEQ. ID. NO. 17 P K Q D A E A A K R F I L D M Y T R M Y T G C V D G P E G S

SEQ. ID. NO. 16 R K G S R A R R F F A H F T C A T D T Q S V R S V F K D V R  
SEQ. ID. NO. 17 K K G A R S R R L F S H Y T C A T D T Q N I R K V F K D V R

*FIG. 4a.*

10/III

SEQ. ID. NO. 16 D S V L A R Y L D E I N L L  
SEQ. ID. NO. 17 D S V L A R Y L D E I N L L

*FIG. 4b.*

II/III

## ClustalW Formatted Alignments

SEQ. ID. NO. 18 A T G G C A T T T T A T A G C T G C T G C T G G G  
SEQ. ID. NO. 19 A T G T T G C T G C T G C T G C T A C T G G C G C  
SEQ. ID. NO. 20 A T G G G G C C C G G G G C C C C T T T T G C C C  
SEQ. ID. NO. 21 A T G G C T T C C C C G C G G A G C T C C G G G C

SEQ. ID. NO. 18 T C C T C T T G G C A C T C A C C T G G C A C A C  
SEQ. ID. NO. 19 C A C T C T T C C T C C G C C C C C C G G G C G C  
SEQ. ID. NO. 20 G G G T G G G G T G G C C A C T G C C G C T T C T  
SEQ. ID. NO. 21 A G C C C G G G C C G C - G C C G C C G C C G C C

SEQ. ID. NO. 18 C T C T G C C T A C G G G C C A G A C C A G C G A  
SEQ. ID. NO. 19 G G G C G G G G C G C A G A C C C C C A A C G C C  
SEQ. ID. NO. 20 G G T T G T G A T G G C G G C A G G G G T G G C T  
SEQ. ID. NO. 21 A C C G C C G C C C G C G C G C C T G C T A C T G

SEQ. ID. NO. 18 G C C C A A A A G A A G G G G G A C A T T A T C C  
SEQ. ID. NO. 19 A C C T C A G A A G G T T G C C A G A T C A T A C  
SEQ. ID. NO. 20 C C G G T G T G G G C C T C C C A C T C C C C C C  
SEQ. ID. NO. 21 C T A C T G C T G C T G C C G C T G C T G C T G C

SEQ. ID. NO. 18 T T G G G G G G C T C T T T C C T A T T C A T T T  
SEQ. ID. NO. 19 A C C C G C C C T G G G A A G G G G G C A T C A G  
SEQ. ID. NO. 20 A T C T C C C G C G G C C T C A C T C G C G G G T  
SEQ. ID. NO. 21 C T C T G G C G C C C G G G G C C T G G G G C T G

SEQ. ID. NO. 18 T G G A G T A G C A G C T A A A G A T C A A G A T  
SEQ. ID. NO. 19 G T A C C G G G G C C T G A C T C G G G A C C A G  
SEQ. ID. NO. 20 C C C C C G C A C C C C T C C T C A G A A C G G  
SEQ. ID. NO. 21 G G C G C G G G G C G C C C C C C G G C C G C C G

SEQ. ID. NO. 18 C T C A A A T C A A G G C C G G A G T C T G T G G  
SEQ. ID. NO. 19 G T G A A G G C T A T C A A C T T C C T G C C A G  
SEQ. ID. NO. 20 C G C G C A G T G T A C A T C G G G G C A C T G T  
SEQ. ID. NO. 21 C C C A G C A G C C C G C C G C T C T C C A T C A

SEQ. ID. NO. 18 A A T G T A T C A G G T A T A A T T T C C G T G G  
SEQ. ID. NO. 19 T G G A C T A T G A G A T T G A G T A T G T G T G  
SEQ. ID. NO. 20 T T C C C A T G A G C G G G G G C T G G C C A G G  
SEQ. ID. NO. 21 T G G G C C T C A T G C C G C T C A C C A A G G A

FIG. 5a.

12/III

SEQ. ID. NO. 18 G T T T C G C T G G T T A C A G G C T A T G A T A  
SEQ. ID. NO. 19 C C G G G G G G A G C G C G A G G T G G T G G G G  
SEQ. ID. NO. 20 G G G C C A G G C C T G C C A G C C C G C G G T G  
SEQ. ID. NO. 21 G G T G G C C A A G G G C A G C A T C G G G C G C

SEQ. ID. NO. 18 T T T G C C A T A G A G G A G A T A A A C A G C A  
SEQ. ID. NO. 19 C C C A A G G T C C G C A A G T G C C T G G C C A  
SEQ. ID. NO. 20 G A G A T G G C G C T G G A G G A C G T G A A T A  
SEQ. ID. NO. 21 G G T G T G C T C C C C G C C G T G G A A C T G G

SEQ. ID. NO. 18 G C C C A G C C C T T C T T C C C A A C T T G A C  
SEQ. ID. NO. 19 A C G G C T C C T G G A C A G A T A T G G A C A C  
SEQ. ID. NO. 20 G C C G C A G G G A C A T C C T G C C G G A C T A  
SEQ. ID. NO. 21 C C A T C G A G C A G A T C C G C A A C G A G T C

SEQ. ID. NO. 18 G C T G G G A T A C A G G A T A T T T G A C A C T  
SEQ. ID. NO. 19 A C C C A G C C G C T G T G T C C G A A T C T G C  
SEQ. ID. NO. 20 T G A G C T C A A G C T C A T C C A C C A C G A C  
SEQ. ID. NO. 21 A C T C C T G C G C C C C T A C T T C C T C G A C

SEQ. ID. NO. 18 T G C A A C A C C G T T T C T A A G G C C T T G G  
SEQ. ID. NO. 19 T C C A A G T C T T A T T T G A C C C T G G A A A  
SEQ. ID. NO. 20 A G C A A G T G T G A T C C A G G C C A A G C C A  
SEQ. ID. NO. 21 C T G C G G C T C T A T G A C A C G G A G T G C G

SEQ. ID. NO. 18 A A G C C A C C C T G A G T T T T G T T G C T C A  
SEQ. ID. NO. 19 A T G G G A A G G T T T T C C T G A C G G G T G G  
SEQ. ID. NO. 20 C C A A G T A C C T A T A T G A G C T G C T C T A  
SEQ. ID. NO. 21 A C A A C G C A A A A G G G T T G A A A G C C T T

SEQ. ID. NO. 18 A A A C A A A A T T G A T T C T T T G A A C C T T  
SEQ. ID. NO. 19 G G A C C T C C C A G C T C T G G A C G G A G C C  
SEQ. ID. NO. 20 C A A C G A C C C T A T C A A G A T C A T C C T T  
SEQ. ID. NO. 21 C T A C G A T G C A A T A A A A T A C G G G C C G

SEQ. ID. NO. 18 G A T G A G T T C T G C A A C T G C T C A G A G C  
SEQ. ID. NO. 19 C G G G T G G A T T T C C G G T G T G A C C C C G  
SEQ. ID. NO. 20 A T G C C T G G C T G C A G C T C T G T C T C C A  
SEQ. ID. NO. 21 A A C C A C T T G A T G G T G T T T G G A G G C G

*FIG. 5b.*

13/III

SEQ. ID. NO. 18 A C A T T C C C T C T A C G A T T G C T G T G G T  
SEQ. ID. NO. 19 A C T T C C A T C T G G T G G G C A G C T C C C G  
SEQ. ID. NO. 20 C G C T G G T G G C T G A G G C T G C T A G G A T  
SEQ. ID. NO. 21 T C T G T C C A T C C G T C A C A T C C A T C A T

SEQ. ID. NO. 18 G G G A G C A A C T G G C T C A G G C G T C T C C  
SEQ. ID. NO. 19 G A G C A T C T G T A G T C A G G G C C A G T G G  
SEQ. ID. NO. 20 G T G G A A C C T C A T T G T G C T T T C C T A T  
SEQ. ID. NO. 21 T G C A G A G T C C C T C C A A G G C T G G A A T

SEQ. ID. NO. 18 A C G G C A G T G G C A A A T C T G C T G G G G C  
SEQ. ID. NO. 19 A G C A C C C C C A A G C C C C A C T G C C A G G  
SEQ. ID. NO. 20 G G C T C C A G C T C A C C A G C C C T G T C A A  
SEQ. ID. NO. 21 C T G G T G C A G C T T T C T T T T G C T G C A A

SEQ. ID. NO. 18 T C T T C T A C A T T C C C C A G G T C A G T T A  
SEQ. ID. NO. 19 T G A A T C G A A C G C C A C A C T C A G A A C G  
SEQ. ID. NO. 20 A C C G G C A G C G T T T C C C C A C T T T T C T T  
SEQ. ID. NO. 21 C C A C G C C T G T T C T A G C C G A T A A G A A

SEQ. ID. NO. 18 T G C C T C C T C C A G C A G A C T C C T C A G C  
SEQ. ID. NO. 19 G C G C G C A G T G T A C A T C G G G G C A C T G  
SEQ. ID. NO. 20 C C G A A C G C A C C C A T C A G C C A C A C T C  
SEQ. ID. NO. 21 A A A A T A C C C T T A T T T C T T T T C G G A C C

SEQ. ID. NO. 18 A A C A A G A A T C A A T T C A A G T C T T T C C  
SEQ. ID. NO. 19 T T T C C C A T G A G C G G G G G C T G G C C A G  
SEQ. ID. NO. 20 C A C A A C C C T A C C C G C G T G A A A C T C T  
SEQ. ID. NO. 21 G T C C C A T C A G A C A A T G C G G T G A A T C

SEQ. ID. NO. 18 T C C G A A C C A T C C C C A A T G A T G A G C A  
SEQ. ID. NO. 19 G G G G C C A G G C C T G C C A G C C C G C G G T  
SEQ. ID. NO. 20 T T G A A A A G T G G G G C T G G A A G A A G A T  
SEQ. ID. NO. 21 C A G C C A T T C T G A A G T T G C T C A A G C A

SEQ. ID. NO. 18 C C A G G C C A C T G C C A T G G C A G A C A T C  
SEQ. ID. NO. 19 G G A G A T G G C G C T G G A G G A C G T G A A T  
SEQ. ID. NO. 20 T G C T A C C A T C C A G C A G A C C A C T G A G  
SEQ. ID. NO. 21 C T A C C A G T G G A A G C G C G T G G G C A C G

*FIG. 5c.*

14/III

SEQ. ID. NO. 18 A T C G A G T A T T T C C G C T G G A A C T G G G  
SEQ. ID. NO. 19 A G C C G C A G G G A C A T C C T G C C G G A C T  
SEQ. ID. NO. 20 G T C T T C A C T T T C G A C T C T G G A C G A C C  
SEQ. ID. NO. 21 C T G A C G C A A G A C G T T C A G A G G T T C T

SEQ. ID. NO. 18 T G G G C A C A A T T G C A G C T G A T G A C G A  
SEQ. ID. NO. 19 A T G A G C T C A A G C T C A T C C A C C A C G A  
SEQ. ID. NO. 20 T G G A G G A A C G A G T G A A G G A G G C T G G  
SEQ. ID. NO. 21 C T G A G G T G C G G A A T G A C C T G A C T G G

SEQ. ID. NO. 18 C T A T G G G C G G C C G G G G A T T G A G A A A  
SEQ. ID. NO. 19 C A G C A A G T G T G A T C C A G G C C A A G C C  
SEQ. ID. NO. 20 A A T T G A G A T T A C T T T C C G C C A G A G T  
SEQ. ID. NO. 21 A G T T C T G T A T G G C G A G G A C A T T G A G

SEQ. ID. NO. 18 T T C C G A G A G G A A G C T G A G G A A A G G G  
SEQ. ID. NO. 19 A C C A A G T A C C T A T A T G A G C T G C T C T  
SEQ. ID. NO. 20 T T C T T C T C A G A T C C A G C T G T G C C C G  
SEQ. ID. NO. 21 A T T T C A G A C A C C G A G A G C T T C T C C A

SEQ. ID. NO. 18 A T A T C T G C A T C G A C T T C A G T G A A C T  
SEQ. ID. NO. 19 A C A A C G A C C C T A T C A A G A T C A T C C T  
SEQ. ID. NO. 20 T C A A A A A C C T G A A G C G C C A G G A T G C  
SEQ. ID. NO. 21 A C G A T C C C T G T A C C A G T G T C A A A A A

SEQ. ID. NO. 18 C A T C T C C C A G T A C T C T G A T G A G G A A  
SEQ. ID. NO. 19 T A T G C C T G G C T G C A G C T C T G T C T C C  
SEQ. ID. NO. 20 C C G A A T C A T C G T G G G A C T T T T C T A T  
SEQ. ID. NO. 21 G C T G A A G G G G A A T G A T G T G C G G A T C

SEQ. ID. NO. 18 G A G A T C C A G C A T G T G G T A G A G G T G A  
SEQ. ID. NO. 19 A C G C T G G T G G C T G A G G C T G C T A G G A  
SEQ. ID. NO. 20 G A G A C T G A A G C C C G G A A A G T T T T T T  
SEQ. ID. NO. 21 A T C C T T G G C C A G T T T G A C C A G A A T A

SEQ. ID. NO. 18 T T C A A A A T T C C A C G G C C A A A G T C A T  
SEQ. ID. NO. 19 T G T G G A A C C T C A T T G T G C T T T C C T A  
SEQ. ID. NO. 20 G T G A G G T G T A C A A G G A G C G T C T C T T  
SEQ. ID. NO. 21 T G G C A G C A A A A G T G T T C T G T T G T G C

*FIG. 5d.*

15/III

SEQ. ID. NO. 18 C G T G G T T T T C T C C A G T G G C C C A G A T  
SEQ. ID. NO. 19 T G G C T C C A G C T C A C C A G C C C T G T C A  
SEQ. ID. NO. 20 T G G G A A G A A G T A C G T C T G G T T C C T C  
SEQ. ID. NO. 21 A T A C G A G G A G A A C A T G T A T G G T A G T

SEQ. ID. NO. 18 C T T G A G C C C C T C A T C A A G G A G A T T G  
SEQ. ID. NO. 19 A A C C G G C A G C G T T T C C C C A C T T T C T  
SEQ. ID. NO. 20 A T T G G G T G G T A T G C T G A C A A T T G G T  
SEQ. ID. NO. 21 A A A T A T C A G T G G A T C A T T C C G G G C T

SEQ. ID. NO. 18 T C C G G C G C A A T A T C A C G G G C A A G A T  
SEQ. ID. NO. 19 T C C G A A C G C A C C C A T C A G C C A C A C T  
SEQ. ID. NO. 20 T C A A G A T C T A C G A C C C T T C T A T C A A  
SEQ. ID. NO. 21 G G T A C G A G C C T T C T T G G T G G G A G C A

SEQ. ID. NO. 18 C T G G C T G G C C A G C G A G G C C T G G G C C  
SEQ. ID. NO. 19 C C A C A A C C C T A C C C G C G T G A A A C T C  
SEQ. ID. NO. 20 C T G C A C A G T G G A T G A G A T G A C T G A G  
SEQ. ID. NO. 21 G G T G C A C A C G G A A G C C A A C T C A T C C

SEQ. ID. NO. 18 A G C T C C T C C C T G A T C G C C A T G C C T C  
SEQ. ID. NO. 19 T T T G A A A A G T G G G G C T G G A A G A A G A  
SEQ. ID. NO. 20 G C G G T G G A G G G C C A C A T C A C A A C T G  
SEQ. ID. NO. 21 C G C T G C C T C C G G A A G A A T C T G C T T G

SEQ. ID. NO. 18 A G T A C T T C C A C G T G G T T G G C G G C A C  
SEQ. ID. NO. 19 T T G C T A C C A T C C A G C A G A C C A C T G A  
SEQ. ID. NO. 20 A G A T T G T C A T G C T G A A T C C T G C C A A  
SEQ. ID. NO. 21 C T G C C A T G G A G G G C T A C A T T G G C G T

SEQ. ID. NO. 18 C A T T G G A T T C G C T C T G A A G G C T G G G  
SEQ. ID. NO. 19 G G T C T T C A C T T C G A C T C T G G A C G A C  
SEQ. ID. NO. 20 T A C C C G C A G C A T T T C C A A C A T G A C A  
SEQ. ID. NO. 21 G G A T T T C G A G C C C C T G A G C T C C A A G

SEQ. ID. NO. 18 C A G A T C C C A G G C T T C C G G G A A T T C C  
SEQ. ID. NO. 19 C T G G A G G A A C G A G T G A A G G A G G C T G  
SEQ. ID. NO. 20 T C C C A G G A A T T T G T G G A G A A A C T A A  
SEQ. ID. NO. 21 C A G A T C A A G A C C A T C T C A G G A A A G A

*FIG. 5e.*

16/III

SEQ. ID. NO. 18 T G A A G A A G G T C C A T C C C A G G A A G T C  
SEQ. ID. NO. 19 G A A T T G A G A T T A C T T T C C G C C A G A G  
SEQ. ID. NO. 20 C C A A G C G A C T G A A A G A C A C C C T G A  
SEQ. ID. NO. 21 C T C C A C A G C A G T A T G A G A G A G A G T A

SEQ. ID. NO. 18 T G T C C A C A A T G G T T T T G C C A A G G A G  
SEQ. ID. NO. 19 T T T C T T C T C A G A T C C A G C T G T G C C C  
SEQ. ID. NO. 20 G G A G A C A G G A G G C T T C C A G G A G G C A  
SEQ. ID. NO. 21 C A A C A A C A A G C G G T C A G G C G T G G G G

SEQ. ID. NO. 18 T T T T G G G A A G A A A C A T T T A A C T G C C  
SEQ. ID. NO. 19 G T C A A A A A C C T G A A G C G C C A G G A T G  
SEQ. ID. NO. 20 C C G C T G G C C T A T G A T G C C A T C T G G G  
SEQ. ID. NO. 21 C C C A G C A A G T T C C A C G G G T A C G C C T

SEQ. ID. NO. 18 A C C T C C A A G A A G G T G C A A A A G G A C C  
SEQ. ID. NO. 19 C C C G A A T C A T C G T G G G A C T T T T T C T A  
SEQ. ID. NO. 20 C C T T G G C A C T G G C C C T G A A C A A G A C  
SEQ. ID. NO. 21 A C G A T G G C A T C T G G G T C A T C G C C A A

SEQ. ID. NO. 18 T T T A C C T G T G G A C A C C T T T C T G A G A  
SEQ. ID. NO. 19 T G A G A C T G A A G C C C G G A A A G T T T T T  
SEQ. ID. NO. 20 A T C T G G A G G A G G C G G C C G T T C T G G T  
SEQ. ID. NO. 21 G A C A C T G C A G A G G G C C A T G G A G A C A

SEQ. ID. NO. 18 G G T C A C G A A G A A A G T G G C G A C A G G T  
SEQ. ID. NO. 19 T G T G A G G T G T A C A A G G A G C G T C T C T  
SEQ. ID. NO. 20 G T G C G C C T G G A G G A C T T C A A C T A C A  
SEQ. ID. NO. 21 C T G C A T G C C A G C A G C C G G C A C C A G C

SEQ. ID. NO. 18 T T A G C A A C A G C T C G A C A G C C T T C C G  
SEQ. ID. NO. 19 T T G G G A A G A A G T A C G T C T G G T T C C T  
SEQ. ID. NO. 20 A C A A C C A G A C C A T T A C C G A C C A A A T  
SEQ. ID. NO. 21 G G A T C C A G G A C T T C A A C T A C A C G G A

SEQ. ID. NO. 18 A C C C C T C T G T A C A G G G G A T G A G A A C  
SEQ. ID. NO. 19 C A T T G G G T G G T A T G C T G A C A A T T G G  
SEQ. ID. NO. 20 C T A C C G G G C A A T G A A C T C T T C G T C C  
SEQ. ID. NO. 21 C C A C A C G C T G G G C A G G A T C A T C C T C

*FIG. 5f.*



17/III

SEQ. ID. NO. 18 A T C A G C A G T G T C G A G A C C C C T T A C A  
SEQ. ID. NO. 19 T T C A A G A T C T A C G A C C C T T C T A T C A  
SEQ. ID. NO. 20 T T T G A G G G T G T C T C T G G C C A T G T G G  
SEQ. ID. NO. 21 A A T G C C A T G A A C G A G A C C A A C T T C T

SEQ. ID. NO. 18 T A G A T T A C A C G C A T T T A C G G A T A T C  
SEQ. ID. NO. 19 A C T G C A C A G T G G A T G A G A T G A C T G A  
SEQ. ID. NO. 20 T G T T T G A T G C C A G C G G C T C T C G G A T  
SEQ. ID. NO. 21 T C G G G G T C A C G G G T C A A G T T G T A T T

SEQ. ID. NO. 18 C T A C A A T G T G T A C T T A G C A G T C T A C  
SEQ. ID. NO. 19 G G C G G T G G A G G G C C A C A T C A C A A C T  
SEQ. ID. NO. 20 G G C A T G G A C G C T T A T C G A G C A G C T T  
SEQ. ID. NO. 21 C C G G A A T G G G G A G A G A A T G G G G A C C

SEQ. ID. NO. 18 T C C A T T G C C C A C G C C T T G C A A G A T A  
SEQ. ID. NO. 19 G A G A T T G T C A T G C T G A A T C C T G C C A  
SEQ. ID. NO. 20 C A G G G T G G C A G C T A C A A G A A G A T T G  
SEQ. ID. NO. 21 A T T A A A T T T A C T C A A T T T C A A G A C A

SEQ. ID. NO. 18 T A T A T A C C T G C T T A C C T G G G A G A G G  
SEQ. ID. NO. 19 A T A C C C G C A G C A T T T C C A A C A T G A C  
SEQ. ID. NO. 20 G C T A C T A T G A C A G C A C C A A G G A T G A  
SEQ. ID. NO. 21 G C A G G G A G G T G A A G G T G G G A G A G T A

SEQ. ID. NO. 18 G C T C T T C A C C A A T G G C T C C T G T G C A  
SEQ. ID. NO. 19 A T C C C A G G A A T T T G T G G A G A A A C T A  
SEQ. ID. NO. 20 T C T T T C C T G G T C C A A A A C A G A T A A A  
SEQ. ID. NO. 21 C A A C G C T G T G G C C G A C A C A C T G G A G

SEQ. ID. NO. 18 G A C A T C A A G A A A G T T G A G G C G T G G C  
SEQ. ID. NO. 19 A C C A A G C G A C T G A A A A G A C A C C C T G  
SEQ. ID. NO. 20 T G G A T T G G A G G G T C C C C C C A G C T G  
SEQ. ID. NO. 21 A T C A T C A A T G A C A C C A T C A G G T T C C

SEQ. ID. NO. 18 A G G T C C T G A A G C A C C T A C G G C A T C T  
SEQ. ID. NO. 19 A G G A G A C A G G A G G C T T C C A G G A G G C  
SEQ. ID. NO. 20 A C C A G A C C C T G G T C A T C A A G A C A T T  
SEQ. ID. NO. 21 A A G G A T C C G A A C C A C C A A A A G A C A A

*FIG. 5g.*

18/III

SEQ. ID. NO. 18 A A A C T T T A C A A A C A A T A T G G G G G A G  
SEQ. ID. NO. 19 A C C G C T G G C C T A T G A T G C C A T C T G G  
SEQ. ID. NO. 20 C C G C T T C C T G T C A C A G A A A C T C T T T  
SEQ. ID. NO. 21 G A C C A T C A T C C T G G A G C A G C T G C G G

SEQ. ID. NO. 18 C A G G T G A C C T T T G A T G A G T G T G G T G  
SEQ. ID. NO. 19 G C C T T G G C A C T G G C C C T G A A C A A G A  
SEQ. ID. NO. 20 A T C T C C G T C T C A G T T C T C T C C A G C C  
SEQ. ID. NO. 21 A A G A T C T C C C T A C C T C T C T A C A G C A

SEQ. ID. NO. 18 A C C T G G T G G G G A A C T A T T C C A T C A T  
SEQ. ID. NO. 19 C A T C T G G A G G A G G C G G C C G T T C T G G  
SEQ. ID. NO. 20 T G G G C A T T G T C C T A G C T G T T G T C T G  
SEQ. ID. NO. 21 T C C T C T C T G C C C T C A C C A T C C T C G G

SEQ. ID. NO. 18 C A A C T G G C A C C T C T C C C C A G A G G A T  
SEQ. ID. NO. 19 T G T G C G C C T G G A G G A C T T C A A C T A C  
SEQ. ID. NO. 20 T C T G T C C T T T A A C A T C T A C A A C T C A  
SEQ. ID. NO. 21 G A T G A T C A T G G C C A G T G C T T T T C T C

SEQ. ID. NO. 18 G G C T C C A T C G T G T T T A A G G A A G T C G  
SEQ. ID. NO. 19 A A C A A C C A G A C C A T T A C C G A C C A A A  
SEQ. ID. NO. 20 C A T G T C C G T T A T A T C C A G A A C T C A C  
SEQ. ID. NO. 21 T T C T T C A A C A T C A A G A A C C G G A A T C

SEQ. ID. NO. 18 G G T A T T A C A A C G T C T A T G C C A A G A A  
SEQ. ID. NO. 19 T C T A C C G G G C A A T G A A C T C T T C G T C  
SEQ. ID. NO. 20 A G C C C A A C C T G A A C A A C C T G A C T G C  
SEQ. ID. NO. 21 A G A A G C T C A T A A A G A T G T C G A G T C C

SEQ. ID. NO. 18 G G G A G A A A G A C T C T T C A T C A A C G A G  
SEQ. ID. NO. 19 C T T T G A G G G T G T C T C T G G C C A T G T G  
SEQ. ID. NO. 20 T G T G G G C T G C T C A C T G G C T T T A G C T  
SEQ. ID. NO. 21 A T A C A T G A A C A A C C T T A T C A T C C T T

SEQ. ID. NO. 18 G A G A A A A T C C T G T G G A G T G G G T T C T  
SEQ. ID. NO. 19 G T G T T T G A T G C C A G C G G C T C T C G G A  
SEQ. ID. NO. 20 G C T G T C T T C C C C C T G G G G C T C G A T G  
SEQ. ID. NO. 21 G G A G G G A T G C T C T C C T A T G C T T C C A

*FIG. 5h.*

19/III

SEQ. ID. NO. 18 C C A G G G A G G T G C C C T T C T C C A A C T G  
SEQ. ID. NO. 19 T G G C A T G G A C G C T T A T C G A G C A G C T  
SEQ. ID. NO. 20 G T T A C C A C A T T G G G A G G A A C C A G T T  
SEQ. ID. NO. 21 T A T T T C T C T T T G G C C T T G A T G G A T C

SEQ. ID. NO. 18 C A G C C G A G A C T G C C T G G C A G G G A C C  
SEQ. ID. NO. 19 T C A G G G T G G C A G C T A C A A G A A G A T T  
SEQ. ID. NO. 20 T C C T T T C G T C T G C C A G G C C C G C C T C  
SEQ. ID. NO. 21 C T T T G T C T C T G A A A A G A C C T T T G A A

SEQ. ID. NO. 18 A G G A A A G G G A T C A T T G A G G G G G A G C  
SEQ. ID. NO. 19 G G C T A C T A T G A C A G C A C C A A G G A T G  
SEQ. ID. NO. 20 T G G C T C C T G G G C C T G G G C T T T A G T C  
SEQ. ID. NO. 21 A C A C T T T G C A C C G T C A G G A C C T G G A

SEQ. ID. NO. 18 C C A C C T G C T G C T T T G A G T G T G T G G A  
SEQ. ID. NO. 19 A T C T T T C C T G G T C C A A A A C A G A T A A  
SEQ. ID. NO. 20 T G G G C T A C G G T T C C A T G T T C A C C A A  
SEQ. ID. NO. 21 T T C T C A C C G T G G G C T A C A C G A C C G C

SEQ. ID. NO. 18 G T G T C C T G A T G G G G A G T A T A G T G A T  
SEQ. ID. NO. 19 A T G G A T T G G A G G G T C C C C C C C A G C T  
SEQ. ID. NO. 20 G A T T T G G T G G G T C C A C A C G G T C T T C  
SEQ. ID. NO. 21 T T T T G G G G C C A T G T T T G C A A A G A C C

SEQ. ID. NO. 18 G A G A C A G A T G C C A G T G C C T G T A A C A  
SEQ. ID. NO. 19 G A C C A G A C C C T G G T C A T C A A G A C A T  
SEQ. ID. NO. 20 A C A A A G A A G G A A G A A A A G A A G G A G T  
SEQ. ID. NO. 21 T G G A G A G T C C A C G C C A T C T T C A A A A

SEQ. ID. NO. 18 A G T G C C C A G A T G A C T T C T G G T C C A A  
SEQ. ID. NO. 19 T C C G C T T C C T G T C A C A G A A A C T C T T  
SEQ. ID. NO. 20 G G A G G A A G A C T C T G G A A C C C T G G A A  
SEQ. ID. NO. 21 A T G T G A A A A T G A A G A A G A A G A T C A T

SEQ. ID. NO. 18 T G A G A A C C A C A C C T C C T G C A T T G C C  
SEQ. ID. NO. 19 T A T C T C C G T C T C A G T T C T C T C C A G C  
SEQ. ID. NO. 20 G C T G T A T G C C A C A G T G G G C C T G C T G  
SEQ. ID. NO. 21 C A A G G A C C A G A A A C T G C T T G T G A T C

*FIG. 5i.*

20/III

SEQ. ID. NO. 18 A A G G A G A T C G A G T T T C T G T C G T G G A  
SEQ. ID. NO. 19 C T G G G C A T T G T C C T A G C T G T T G T C T  
SEQ. ID. NO. 20 G T G G G C A T G G A T G T C C T C A C T C T C G  
SEQ. ID. NO. 21 G T G G G G G G C A T G C T G C T G A T C G A C C

SEQ. ID. NO. 18 C G G A G C C C T T T G G G A T C G C A C T C A C  
SEQ. ID. NO. 19 G T C T G T C C T T T A A C A T C T A C A A C T C  
SEQ. ID. NO. 20 C C A T C T G G C A G A T C G T G G A C C C T C T  
SEQ. ID. NO. 21 T G T G T A T C C T G A T C T G C T G G C A G G C

SEQ. ID. NO. 18 C C T C T T T G C C G T G C T G G G C A T T T T C  
SEQ. ID. NO. 19 A C A T G T C C G T T A T A T C C A G A A C T C A  
SEQ. ID. NO. 20 G C A C C G G A C C A T T G A G A C A T T T G C C  
SEQ. ID. NO. 21 T G T G G A C C C C C T G C G A A G G A C A G T G

SEQ. ID. NO. 18 C T G A C A G C C T T T G T G C T G G G T G T G T  
SEQ. ID. NO. 19 C A G C C C A A C C T G A A C A A C C T G A C T G  
SEQ. ID. NO. 20 A A G G A G G A A C C T A A G G A A G A T A T T G  
SEQ. ID. NO. 21 G A G A A G T A C A G C A T G G A G C C G G A C C

SEQ. ID. NO. 18 T T A T C A A G T T C C G C A A C A C A C C C A T  
SEQ. ID. NO. 19 C T G T G G G C T G C T C A C T G G C T T T A G C  
SEQ. ID. NO. 20 A C G T C T C T A T T C T G C C C C A G C T G G A  
SEQ. ID. NO. 21 C A G C A G G A C G G G A T A T C T C C A T C C G

SEQ. ID. NO. 18 T G T C A A G G C C A C C A A C C G A G A G C T C  
SEQ. ID. NO. 19 T G C T G T C T T C C C C C T G G G G C T C G A T  
SEQ. ID. NO. 20 G C A T T G C A G C T C C A G G A A G A T G A A T  
SEQ. ID. NO. 21 C C C T C T C C T G G A G C A C T G T G A G A A C

SEQ. ID. NO. 18 T C C T A C C T C C T C C T C T T C T C C C T G C  
SEQ. ID. NO. 19 G G T T A C C A C A T T G G G A G G A A C C A G T  
SEQ. ID. NO. 20 A C A T G G C T T G G C A T T T T C T A T G G T T  
SEQ. ID. NO. 21 A C C C A T A T G A C C A T C T G G C T T G G C A

SEQ. ID. NO. 18 T C T G C T G C T T C T C C A G C T C C C T G T T  
SEQ. ID. NO. 19 T T C C T T T C G T C T G C C A G G C C C G C C T  
SEQ. ID. NO. 20 A C A A G G G G C T G C T G C T G C T G G G  
SEQ. ID. NO. 21 T C G T C T A T G C C T A C A A G G G A C T T C T

*FIG. 5j.*

SUBSTITUTE SHEET (RULE 26)

21/III

SEQ. ID. NO. 18 C T T C A T C G G G G A G C C C C A G G A C T G G  
SEQ. ID. NO. 19 C T G G C T C C T G G G C C T G G G C T T T A G T  
SEQ. ID. NO. 20 A A T C T T C C T T G C T T A T G A G A C C A A G  
SEQ. ID. NO. 21 C A T G T T G T T C G G T T G T T T C T T A G C T

SEQ. ID. NO. 18 A C G T G C C G C C T G C G C C A G C C G G C C T  
SEQ. ID. NO. 19 C T G G G C T A C G G T T C C A T G T T C A C C A  
SEQ. ID. NO. 20 A G T G T G T C C A C T G A G A A G A T C A A T G  
SEQ. ID. NO. 21 T G G G A G A C C C G C A A C G T C A G C A T C C

SEQ. ID. NO. 18 T T G G C A T C A G C T T C G T G C T C T G C A T  
SEQ. ID. NO. 19 A G A T T T G G T G G G T C C A C A C G G T C T T  
SEQ. ID. NO. 20 A T C A C C G G G C T G T G G G C A T G G C T A T  
SEQ. ID. NO. 21 C C G C A C T C A A C G A C A G C A A G T A C A T

SEQ. ID. NO. 18 C T C A T G C A T C C T G G T G A A A A C C A A C  
SEQ. ID. NO. 19 C A C A A A G A A G G A A G A A A A G A A G G A G  
SEQ. ID. NO. 20 C T A C A A T G T G G C A G T C C T G T G C C T C  
SEQ. ID. NO. 21 C G G G A T G A G T G T C T A C A A C G T G G G G

SEQ. ID. NO. 18 C G T G T C C T C C T G G T G T T T G A G G C C A  
SEQ. ID. NO. 19 T G G A G G A A G A C T C T G G A A C C C T G G A  
SEQ. ID. NO. 20 A T C A C T G C T C C T G T C A C C A T G A T T C  
SEQ. ID. NO. 21 A T C A T G T G C A T C A T C G G G G C C G C T G

SEQ. ID. NO. 18 A G A T C C C C A C C A G C T T C C A C C G C A A  
SEQ. ID. NO. 19 A G C T G T A T G C C A C A G T G G G C C T G C T  
SEQ. ID. NO. 20 T G T C C A G C C A G C A G G A T G C A G C C T T  
SEQ. ID. NO. 21 T C T C C T T C C T G A C C C G G G A C C A G C C

SEQ. ID. NO. 18 G T G G T G G G G G C T C A A C C T G C A G T T C  
SEQ. ID. NO. 19 G G T G G G C A T G G A T G T C C T C A C T C T C  
SEQ. ID. NO. 20 T G C C T T T G C C T C T C T T G C C A T A G T T  
SEQ. ID. NO. 21 C A A T G T G C A G T T C T G C A T C G T G G C T

SEQ. ID. NO. 18 C T G C T G G T T T T C C T C T G C A C C T T C A  
SEQ. ID. NO. 19 G C C A T C T G G C A G A T C G T G G A C C C T C  
SEQ. ID. NO. 20 T T C T C C T C C T A T A T C A C T C T T G T T G  
SEQ. ID. NO. 21 C T G G T C A T C A T C T T C T G C A G C A C C A

*FIG. 5k.*

22/III

SEQ. ID. NO. 18 T G C A G A T T G T C A T C T G T G T G A T C T G  
SEQ. ID. NO. 19 T G C A C C G G A C C A T T G A G A C A T T T G C  
SEQ. ID. NO. 20 T G C T C T T T G T G C C C A A G A T G C G C A G  
SEQ. ID. NO. 21 T C A C C C T C T G C C T G G T A T T C G T G C C

SEQ. ID. NO. 18 G C T C T A C A C C G C G C C C C C C T C A A G C  
SEQ. ID. NO. 19 C A A G G A G G A A C C T A A G G A A G A T A T T  
SEQ. ID. NO. 20 G C T G A T C A C C C G A G G G G A A T G G C A G  
SEQ. ID. NO. 21 G A A G C T C A T C A C C C T G A G A A C A A A C

SEQ. ID. NO. 18 T A C C G C A A C C A G G A G C T G G A G G A T G  
SEQ. ID. NO. 19 G A C G T C T C T A T T C T G C C C C A G C T G G  
SEQ. ID. NO. 20 T C G G A G G C G C A G G A C A C C A T G A A G A  
SEQ. ID. NO. 21 C C A G A T G C A G C A A C G C A G A A C A G G C

SEQ. ID. NO. 18 A G A T C A T C T T C A T C A C G T G C C A C G A  
SEQ. ID. NO. 19 A G C A T T G C A G C T C C A G G A A G A T G A A  
SEQ. ID. NO. 20 C A G G G T C A T C G A C C A A C A A C A A C G A  
SEQ. ID. NO. 21 G A T T C C A G T T C A C T C A G A A T C A G A A

SEQ. ID. NO. 18 G G G C T C C C T C A T G G C C C T G G G C T T C  
SEQ. ID. NO. 19 T A C A T G G C T T G G C A T T T T C T A T G G T  
SEQ. ID. NO. 20 G G A G G A G A A G T C C C G G C T G T T G G A G  
SEQ. ID. NO. 21 G A A A G A A G A T T C T A A A A C G T C C A C C

SEQ. ID. NO. 18 C T G A T C G G C T A C A C C T G C C T G C T G G  
SEQ. ID. NO. 19 T A C A A G G G G C T G C T G C T G C T G C T G G  
SEQ. ID. NO. 20 A A G G A G A A C C G T G A A C T G G A A A A G A  
SEQ. ID. NO. 21 T C G G T C A C C A G T G T G A A C C A A G C C A

SEQ. ID. NO. 18 C T G C C A T C T G C T T C T T C T T T G C C T T  
SEQ. ID. NO. 19 G A A T C T T C C T T G C T T A T G A G A C C A A  
SEQ. ID. NO. 20 T C A T T G C T G A G A A A G A G G A G C G T G T  
SEQ. ID. NO. 21 G C A C A T C C C G C C T G G A G G G C C T A C A

SEQ. ID. NO. 18 C A A G T C C C G G A A G C T G C C G G A G A A C  
SEQ. ID. NO. 19 G A G T G T G T C C A C T G A G A A G A T C A A T  
SEQ. ID. NO. 20 C T C T G A A C T G C G C C A T C A A C T C C A G  
SEQ. ID. NO. 21 G T C A G A A A A C C A T C G C C T G C G A A T G

FIG. 5L.

SUBSTITUTE SHEET (RULE 26)

23/III

SEQ. ID. NO. 18 T T C A A T G A A G C C A A G T T C A T C A C C T  
SEQ. ID. NO. 19 G A T C A C C G G G C T G T G G G C A T G G C T A  
SEQ. ID. NO. 20 T C T C G G C A G C A G C T C C G C T C C C G G C  
SEQ. ID. NO. 21 A A G A T C A C A G A G C T G G A T A A A G A C T

SEQ. ID. NO. 18 T C A G C A T G C T C A T C T T C T T C A T C G T  
SEQ. ID. NO. 19 T C T A C A A T G T G G C A G T C C T G T G C C T  
SEQ. ID. NO. 20 G C C A C C C A C C G A C A C C C C C A G A A C C  
SEQ. ID. NO. 21 T G G A A G A G G T C A C C A T G C A G C T G C A

SEQ. ID. NO. 18 C T G G A T C T C C T T C A T T C C A G C C T A T  
SEQ. ID. NO. 19 C A T C A C T G C T C C T G T C A C C A T G A T T  
SEQ. ID. NO. 20 C T C T G G G G G C C T G C C C A G G G G A C C C  
SEQ. ID. NO. 21 G G A C A C A C C A G A A A A G A C C A C C T A C

SEQ. ID. NO. 18 G C C A G C A C C T A T G G C A A G T T T G T C T  
SEQ. ID. NO. 19 C T G T C C A G C C A G C A G G A T G C A G C C T  
SEQ. ID. NO. 20 C C T G A G C C C C C C G A C C G G C T T A G C T  
SEQ. ID. NO. 21 A T T A A A C A G A A C C A C T A C C A A G A G C

SEQ. ID. NO. 18 C T G C C G T A G A G G T G A T T G C C A T C C T  
SEQ. ID. NO. 19 T T G C C T T T G C C T C T C T T G C C A T A G T  
SEQ. ID. NO. 20 G T G A T G G G A G T C G A G T G C A T T T G C T  
SEQ. ID. NO. 21 T C A A T G A C A T C C T C A A C C T G G G A A A

SEQ. ID. NO. 18 G G C A G C C A G C T T T G G C T T G C T G G C G  
SEQ. ID. NO. 19 T T T C T C C T C C T A T A T C A C T C T T G T T  
SEQ. ID. NO. 20 T T A T A A G T G A G G G T A G G G T G A G G G A  
SEQ. ID. NO. 21 C T T C A C T G A G A G C A C A G A T G G A G G A

SEQ. ID. NO. 18 T G C A T C T T C T T C A A C A A G A T C T A C A  
SEQ. ID. NO. 19 G T G C T C T T T G T G C C C A A G A T G C G C A  
SEQ. ID. NO. 20 G G A C A G G C C A G T A G G G G G A G G G A A A  
SEQ. ID. NO. 21 A A G G C C A T T T T A A A A A A T C A C C T C G

SEQ. ID. NO. 18 T C A T T C T C T T C A A G C C A T C C C G C A A  
SEQ. ID. NO. 19 G G C T G A T C A C C C G A G G G G A A T G G C A  
SEQ. ID. NO. 20 G G G A G A G G G G A A G G G C A G G G G A C T C  
SEQ. ID. NO. 21 A T C A A A A T C C C C A G C T A C A G T G G A A

*FIG. 5m.*

24/III

SEQ. ID. NO. 18 C A C C A T C G A G G A G G T G C G T T G C A G C  
SEQ. ID. NO. 19 G T C G G A G G C G C A G G A C A C C A T G A A G  
SEQ. ID. NO. 20 A G G A A G C A G G G G G T C C C C A T C C C C A  
SEQ. ID. NO. 21 C A C A A C A G A G C C C T C T C G A A C A T G C

SEQ. ID. NO. 18 A C C G C A G C T C A C G C T T T C A A G G T G G  
SEQ. ID. NO. 19 A C A G G G T C A T C G A C C A A C A A C A A C G  
SEQ. ID. NO. 20 G C T G G G A A G A A C A T G C T A T C C A A T C  
SEQ. ID. NO. 21 A A A G A T C C T A T A G A A G A T A T A A A C T

SEQ. ID. NO. 18 C T G C C C G G G C C A C G C T G C G C C G C A G  
SEQ. ID. NO. 19 A G G A G G A G A A G T C C C G G C T G T T G G A  
SEQ. ID. NO. 20 T C A T C T C T T G T A A A T A C A T G T C C C C  
SEQ. ID. NO. 21 C T C C A G A A C A C A T C C A G C G T C G G C T

SEQ. ID. NO. 18 C A A C G T C T C C C G C A A G C G G T C C A G C  
SEQ. ID. NO. 19 G A A G G A G A A C C G T G A A C T G G A A A A G  
SEQ. ID. NO. 20 C T G T G A G T T C T G G G C T G A T T T G G G T  
SEQ. ID. NO. 21 G T C C C T C C A G C T C C C C A T C C T C C A C

SEQ. ID. NO. 18 A G C C T T G G A G G C T C C A C G G G A T C C A  
SEQ. ID. NO. 19 A T C A T T G C T G A G A A A G A G G A G C G T G  
SEQ. ID. NO. 20 C T C T C A T A C C T C T G G G A A A C A G A C C  
SEQ. ID. NO. 21 C A C G C C T A C C T C C C A T C C A T C G G A G

SEQ. ID. NO. 18 C C C C C T C C T C C T C C A T C A G C A G C A A  
SEQ. ID. NO. 19 T C T C T G A A C T G C G C C A T C A G C T C C A  
SEQ. ID. NO. 20 T T T T T C T C T C T T A C T G C T T C A T G T A  
SEQ. ID. NO. 21 G C G T G G A C G C C A G C T G T G T C A G C C C

SEQ. ID. NO. 18 G A G C A A C A G C G A A G A C C C A T T C C C A  
SEQ. ID. NO. 19 G T C T C G G C A G C A G C T C C G C T C C C G G  
SEQ. ID. NO. 20 A T T T T G T A T C A C C T C T T C A C A A T T T  
SEQ. ID. NO. 21 C T G C G T C A G C C C C A C C G C C A G C C C C

SEQ. ID. NO. 18 C A G C C C G A G A G G C A G A A G C A G C A G C  
SEQ. ID. NO. 19 C G C C A C C C A C C G A C A C C C C C A G A A C  
SEQ. ID. NO. 20 A G T T C G T A C C T G G C T T G A A G C T G C T  
SEQ. ID. NO. 21 C G C C A C A G A C A T G T G C C A C C C T C C T

*FIG. 5n.*



25/III

SEQ. ID. NO. 18 A G C C G C T G G C C C T A A C C C A G C A A G A  
SEQ. ID. NO. 19 C C T C T G G G G G C C T G C C C A G G G G A C C  
SEQ. ID. NO. 20 C A C T G C T C A C A C G C T G C C T C C T C A G  
SEQ. ID. NO. 21 T C C G A G T C A T G G T C T C G G G C C T G T A

SEQ. ID. NO. 18 G C A G C A G C A G C A G C C C C T G A C C C T C  
SEQ. ID. NO. 19 C C C T G A G C C C C C C G A C C G G C T T A G C  
SEQ. ID. NO. 20 C A G C C T C A C T G C A T C T T T C T C T T C C  
SEQ. ID. NO. 21 A G G G T G G G A G G C C T G G G C C C G G G G C

SEQ. ID. NO. 18 C C A C A G C A G C A A C G A T C T C A G C A G C  
SEQ. ID. NO. 19 T G T G A T G G G A G T C G A G T G C A T T T G C  
SEQ. ID. NO. 20 C A T G C A A C A C C C T C T T C T A G T T A C C  
SEQ. ID. NO. 21 C T C C C C C G T G A C A G A A C C A C A C T G G

SEQ. ID. NO. 18 A G C C C A G A T G C A A G C A G A A G G T C A T  
SEQ. ID. NO. 19 T T T A T A A G T G A G G G T A G G G T G A G G G  
SEQ. ID. NO. 20 A C G G C A A C C C C T  
SEQ. ID. NO. 21 G C A G A G G G G T C T G C T G C A G A A A C A C

SEQ. ID. NO. 18 C T T T G G C A G C G G C A C G G T C A C C T T C  
SEQ. ID. NO. 19 A G G A C A G G C C A G T A G G G G G A G G G A A  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 T G T C G G C T C T G G C T G C G G A G A A G C T

SEQ. ID. NO. 18 T C A C T G A G C T T T G A T G A G C C T C A G A  
SEQ. ID. NO. 19 A G G G A G A G G G G A A G G G C A G G G G A C T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 G G G C A C C A T G G C T G G C C T C T C A G G A

SEQ. ID. NO. 18 A G A A C G C C A T G G C C C A C G G G A A T T C  
SEQ. ID. NO. 19 C A G G A A G C A G G G G G T C C C C A T C C C C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 C C A C T C G G A T G G C A C T C A G G T G G A C

SEQ. ID. NO. 18 T A C G C A C C A G A A C T C C C T G G A G G C C  
SEQ. ID. NO. 19 A G C T G G G A A G A A C A T G C T A T C C A A T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 A G G A C G G G G C A G G G G G A G A C T T G G C

*FIG. 50.*

26/III

SEQ. ID. NO. 18 C A G A A A A G C A G C G A T A C G C T G A C C C  
SEQ. ID. NO. 19 C T C A T C T C T T G T A A A T A C A T G T C C C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 A C C T G A C C T C G A G C C T T A T T T G T G A

SEQ. ID. NO. 18 G A C A C C A G C C A T T A C T C C C G C T G C A  
SEQ. ID. NO. 19 C C T G T G A G T T C T G G G C T G A T T T G G G  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 A G T C C T T A T T T C T T C A C A A A G A A G A

SEQ. ID. NO. 18 G T G C G G G G A A A C G G A C T T A G A T C T G  
SEQ. ID. NO. 19 T C T C T C A T A C C T C T G G G A A A C A G A C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 G G A A C G G A A A T G G G A C G T C T T C C T T

SEQ. ID. NO. 18 A C C G T C C A G G A A A C A G G T C T G C A A G  
SEQ. ID. NO. 19 C T T T T T C T C T C T T A C T G C T T C A T G T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 A A C A T C T G C A A A C A A G G A G G C G C T G

SEQ. ID. NO. 18 G A C C T G T G G G T G G A G A C C A G C G G C C  
SEQ. ID. NO. 19 A A T T T T G T A T C A C C T C T T C A C A A T T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 G G A T A T C A A A C T T G C A A A A A A A A A A

SEQ. ID. NO. 18 A G A G G T G G A G G A C C C T G A A G A G T T G  
SEQ. ID. NO. 19 T A G T T C G T A C C T G G C T T G A A G C T G C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21 A A A A A A A A A A A A

SEQ. ID. NO. 18 T C C C C A G C A C T T G T A G T G T C C A G T T  
SEQ. ID. NO. 19 T C A C T G C T C A C A C G C T G C C T C C T C A  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18 C A C A G A G C T T T G T C A T C A G T G G T G G  
SEQ. ID. NO. 19 G C A G C C T C A C T G C A T C T T T C T C T T C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

*FIG. 5p.*

27/III

SEQ. ID. NO. 18 A G G C A G C A C T G T T A C A G A A A A C G T A  
SEQ. ID. NO. 19 C C A T G C A A C A C C C T C T T C T A G T T A C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18 G T G A A T T C A  
SEQ. ID. NO. 19 C A C G G C A A C C C C T G C A G C T C C T C T G  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 C C T T T G T G C T C T G T T C C T G T C C A G C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 A G G G G T C T C C C A A C A A G T G C T C T T T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 C C A C C C C A A A G G G G C C T C T C C T T T T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 C T C C A C T G T C A T A A T C T C T T T C C A T  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 C T T A C T T G C C C T T C T A T A C T T T T C T C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 A C A T G T G G C T C C C C C T G A A T T T T G C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

*FIG. 5q.*

28/III

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 T T C C T T T G G G G A G C T C A T T C T T T C G  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 C C A A G G T C A C A T G C T C C C T T G C C T C  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

SEQ. ID. NO. 18  
SEQ. ID. NO. 19 T G G C T C C G T G C A  
SEQ. ID. NO. 20  
SEQ. ID. NO. 21

*FIG. 5r.*

29/III

SEQ. ID. NO. 22 A T G C T G C T G C T G C T G C T G G T G C C T C T C T T C  
SEQ. ID. NO. 23 A T G G G C C C G G G G G G A C C C T G T A C C C C A G T G

SEQ. ID. NO. 22 C T C C G C C C C C T G G G C G C T G G C G G G G C G C A G  
SEQ. ID. NO. 23 G G G T G G C C G C T G C C T C T T C T G C T G G T G A T G

SEQ. ID. NO. 22 A C C C C C A A C G C C A C C T C G G A A G G T T G C C A G  
SEQ. ID. NO. 23 G C G G C T G G G G T G G C T C C G G T G T G G G C C T C T

SEQ. ID. NO. 22 A T T A T A C A T C C G C C C T G G G A A G G T G G C A T C  
SEQ. ID. NO. 23 C A C T C C C C T C A T C T C C C G C G G C C T C A C C C G

SEQ. ID. NO. 22 A G G T A C C G T G G C T T G A C T C G C G A C C A G G T G  
SEQ. ID. NO. 23 A G G G T C C C C C C G C A C C C C T C C T C A G A A C G G

SEQ. ID. NO. 22 A A G G C C A T C A A C T T C C T G C C T G T G G A C T A T  
SEQ. ID. NO. 23 C G T G C A G T A T A C A T C G G G G C G C T G T T T C C C

SEQ. ID. NO. 22 G A G A T C G A A T A T G T G T G C C G A G G G G A G C G C  
SEQ. ID. NO. 23 A T G A G C G G G G G C T G G C C G G G G G C C A G G C C

SEQ. ID. NO. 22 G A G G T G G T G G G G C C C A A G G T G C G C A A A T G C  
SEQ. ID. NO. 23 T G C C A G C C C G C G G T G G A G A T G G C G C T G G A G

SEQ. ID. NO. 22 C T G G C C A A C G G C T C C T G G A C G G A T A T G G A C  
SEQ. ID. NO. 23 G A C G T T A A C A G C C G C A G A G A C A T C C T G C C G

SEQ. ID. NO. 22 A C A C C C A G C C G C T G T G T C C G A A T C T G C T C C  
SEQ. ID. NO. 23 G A C T A C G A G C T C A A G C T T A T C C A C C A C G A C

SEQ. ID. NO. 22 A A G T C T T A T T T G A C C C T G G A A A A T G G G A A G  
SEQ. ID. NO. 23 A G C A A G T G T G A C C C A G G G C A A G C C A C C A A G

SEQ. ID. NO. 22 G T T T T C C T G A C G G G T G G G G A C C T C C C A G C T  
SEQ. ID. NO. 23 T A C T T G T A C G A A C T A C T C T A C A A T G A C C C C

FIG. 6a.

30/III

SEQ. ID. NO. 22 C T G G A T G G A G C C C G G G T G G A G T T C C G A T G T  
SEQ. ID. NO. 23 A T C A A G A T C A T T C T C A T G C C T G G C T G T A G T

SEQ. ID. NO. 22 G A C C C C G A C T T C C A T C T G G T G G G C A G C T C C  
SEQ. ID. NO. 23 T C T G T C T C C A C A C T T G T A G C T G A G G C T G C C

SEQ. ID. NO. 22 C G G A G C G T C T G T A G T C A G G G C C A G T G G A G C  
SEQ. ID. NO. 23 C G G A T G T G G A A C C T T A T T G T G C T C T C A T A T

SEQ. ID. NO. 22 A C C C C C A A G C C C C A C T G C C A G G T G A A T C G A  
SEQ. ID. NO. 23 G G C T C C A G T T C A C C A G C C T T G T C A A A C C G A

SEQ. ID. NO. 22 A C G C C A C A C T C A G A A C G G C G T G C A G T A T A C  
SEQ. ID. NO. 23 C A G C G G T T T C C C A C G T T C T T C C G G A C G C A T

SEQ. ID. NO. 22 A T C G G G G C G C T G T T T C C C A T G A G C G G G G G C  
SEQ. ID. NO. 23 C C A T C C G C C A C A C T C C A C A A T C C C A C C C G G

SEQ. ID. NO. 22 T G G C C G G G G G G C C A G G C C T G C C A G C C C G C G  
SEQ. ID. NO. 23 G T G A A A C T C T T C G A A A A G T G G G G C T G G A A G

SEQ. ID. NO. 22 G T G G A G A T G G C G C T G G A G G A C G T T A A C A G C  
SEQ. ID. NO. 23 A A G A T C G C T A C C A T C C A A C A G A C C A C C G A G

SEQ. ID. NO. 22 C G C A G A G A C A T C C T G C C G G A C T A C G A G C T C  
SEQ. ID. NO. 23 G T C T T C A C C T C A A C G C T G G A T G A C C T G G A G

SEQ. ID. NO. 22 A A G C T T A T C C A C C A C G A C A G C A A G T G T G A C  
SEQ. ID. NO. 23 G A G C G A G T G A A A G A G G C T G G G A T C G A G A T C

SEQ. ID. NO. 22 C C A G G G C A A G C C A C C A A G T A C T T G T A C G A A  
SEQ. ID. NO. 23 A C T T T C C G A C A G A G T T T C T T C T C G G A T C C A

SEQ. ID. NO. 22 C T A C T C T A C A A T G A C C C C A T C A A G A T C A T T  
SEQ. ID. NO. 23 G C T G T G C C T G T T A A A A A C C T G A A G C G T C A A

SEQ. ID. NO. 22 C T C A T G C C T G G C T G T A G T T C T G T C T C C A C A  
SEQ. ID. NO. 23 G A T G C T C G A A T C A T C G T G G G A C T T T T C T A T

*FIG. 6b.*

SUBSTITUTE SHEET (RULE 26)

31/III

SEQ. ID. NO. 22 C T T G T A G C T G A G G C T G C C C G G A T G T G G A A C  
SEQ. ID. NO. 23 G A G A C G G A A G C C C G G A A A G T T T T T T G T G A G

SEQ. ID. NO. 22 C T T A T T G T G C T C T C A T A T G G C T C C A G T T C A  
SEQ. ID. NO. 23 G T C T A T A A G G A A A G G C T C T T T G G G A A G A A G

SEQ. ID. NO. 22 C C A G C C T T G T C A A A C C G A C A G C G G T T T C C C  
SEQ. ID. NO. 23 T A C G T C T G G T T C C T C A T C G G G T G G T A T G C T

SEQ. ID. NO. 22 A C G T T C T T C C G G A C G C A T C C A T C C G C C A C A  
SEQ. ID. NO. 23 G A C A A C T G G T T C A A G A C C T A T G A C C C G T C A

SEQ. ID. NO. 22 C T C C A C A A T C C C A C C C G G G T G A A A C T C T T C  
SEQ. ID. NO. 23 A T C A A T T G T A C A G T G G A A G A A A T G A C C G A G

SEQ. ID. NO. 22 G A A A A G T G G G G C T G G A A G A A G A T C G C T A C C  
SEQ. ID. NO. 23 G C G G T G G A G G G C C A C A T C A C C A C G G A G A T T

SEQ. ID. NO. 22 A T C C A A C A G A C C A C C G A G G T C T T C A C C T C A  
SEQ. ID. NO. 23 G T C A T G C T G A A C C C T G C C A A C A C C C G A A G C

SEQ. ID. NO. 22 A C G C T G G A T G A C C T G G A G G A G C G A G T G A A A  
SEQ. ID. NO. 23 A T T T C C A A C A T G A C G T C A C A G G A A T T T G T G

SEQ. ID. NO. 22 G A G G C T G G G A T C G A G A T C A C T T T C C G A C A G  
SEQ. ID. NO. 23 G A G A A A C T A A C C A A G C G G C T G A A A A G A C A C

SEQ. ID. NO. 22 A G T T T C T T C T C G G A T C C A G C T G T G C C T G T T  
SEQ. ID. NO. 23 C C C G A G G A G A C T G G A G G C T T C C A G G A G G C A

SEQ. ID. NO. 22 A A A A A C C T G A A G C G T C A A G A T G C T C G A A T C  
SEQ. ID. NO. 23 C C A C T G G C C T A T G A T G C T A T C T G G G C C T T G

SEQ. ID. NO. 22 A T C G T G G G A C T T T T T C T A T G A G A C G G A A G C C  
SEQ. ID. NO. 23 G C T T T G G C C T T G A A C A A G A C G T C T G G A G G A

SEQ. ID. NO. 22 C G G A A A G T T T T T T G T G A G G T C T A T A A G G A A  
SEQ. ID. NO. 23 G G T G G T C G T T C C G G C G T G C G C C T G G A G G A C

FIG. 6c.

32/III

SEQ. ID. NO. 22 A G G C T C T T T G G G A A G A A G T A C G T C T G G T T C  
SEQ. ID. NO. 23 T T T A A C T A C A A C A A C C A G A C C A T T A C A G A C

SEQ. ID. NO. 22 C T C A T C G G G T G G T A T G C T G A C A A C T G G T T C  
SEQ. ID. NO. 23 C A G A T C T A C C G G G C C A T G A A C T C C T C C T C C

SEQ. ID. NO. 22 A A G A C C T A T G A C C C G T C A A T C A A T T G T A C A  
SEQ. ID. NO. 23 T T T G A G G G C G T T T C T G G C C A T G T G G T C T T T

SEQ. ID. NO. 22 G T G G A A G A A A T G A C C G A G G C G G T G G A G G G C  
SEQ. ID. NO. 23 G A T G C C A G C G G C T C C C G G A T G G C A T G G A C A

SEQ. ID. NO. 22 C A C A T C A C C A C G G A G A T T G T C A T G C T G A A C  
SEQ. ID. NO. 23 C T T A T C G A G C A G C T A C A G G G C G G C A G C T A C

SEQ. ID. NO. 22 C C T G C C A A C A C C C G A A G C A T T T C C A A C A T G  
SEQ. ID. NO. 23 A A G A A G A T C G G C T A C T A C G A C A G C A C C A A G

SEQ. ID. NO. 22 A C G T C A C A G G A A T T T G T G G A G A A A C T A A C C  
SEQ. ID. NO. 23 G A T G A T C T T T C C T G G T C C A A A A C G G A C A A G

SEQ. ID. NO. 22 A A G C G G C T G A A A A G A C A C C C C G A G G A G A C T  
SEQ. ID. NO. 23 T G G A T T G G A G G G T C T C C C C C A G C T G A C C A G

SEQ. ID. NO. 22 G G A G G C T T C C A G G A G G C A C C A C T G G C C T A T  
SEQ. ID. NO. 23 A C C T T G G T C A T C A A G A C A T T C C G T T T C C T G

SEQ. ID. NO. 22 G A T G C T A T C T G G G C C T T G G C T T T G G C C T T G  
SEQ. ID. NO. 23 T C T C A G A A A C T C T T T A T C T C C G T C T C A G T T

SEQ. ID. NO. 22 A A C A A G A C G T C T G G A G G A G G T G G T C G T T C C  
SEQ. ID. NO. 23 C T C T C C A G C C T G G G C A T T G T T C T T G C T G T T

SEQ. ID. NO. 22 G G C G T G C G C C T G G A G G A C T T T A A C T A C A A C  
SEQ. ID. NO. 23 G T C T G T C T G T C C T T T A A C A T C T A C A A C T C C

SEQ. ID. NO. 22 A A C C A G A C C A T T A C A G A C C A G A T C T A C C G G  
SEQ. ID. NO. 23 C A C G T T C G T T A T A T C C A G A A C T C C C A G C C C

*FIG. 6d.*



33/III

SEQ. ID. NO. 22 GCCATGAACTCCTCCTCCTTTGAGGGCGTT  
SEQ. ID. NO. 23 AACCTGAACAATCTGACTGCTGTGGGCTGC

SEQ. ID. NO. 22 TCTGGCCATGTGGTCTTTGATGCCAGCGGGC  
SEQ. ID. NO. 23 TCACTGGCACTGGCTGCTGTCTTCCCTCTC

SEQ. ID. NO. 22 TCCCGGATGGCATGGACACTTATCGAGCAG  
SEQ. ID. NO. 23 GGGCTGGATGGTTACCAACATAGGGAGAAAGC

SEQ. ID. NO. 22 CTACAGGGGCGGCAGCTACAAGAAGATCGGC  
SEQ. ID. NO. 23 CAGTTCCCGTTTGTCTGCCAGGCCCGCCTT

SEQ. ID. NO. 22 TACTACGACAGCACCAAGGATGATCTTTCC  
SEQ. ID. NO. 23 TGGCTCTTGGGCTTGGGCTTTAGTCTGGGC

SEQ. ID. NO. 22 TGGTCCAAAACGGACAAAGTGGATTGGAGGG  
SEQ. ID. NO. 23 TATGGCTCTATGTTCAACCAAGATCTGGGTGG

SEQ. ID. NO. 22 TCTCCCCCAGCTGACCAGACCTTGGGTCATC  
SEQ. ID. NO. 23 GTCCACACAGTCTTTCACGAAGAAGGAGGAG

SEQ. ID. NO. 22 AAGACATTCCGTTTCTCTGTCTCAGAAACTC  
SEQ. ID. NO. 23 AAGAAAGGAGTGGAGGAAGACCCTAGAGCCC

SEQ. ID. NO. 22 TTTATCTCCGTCTCAGTTCTCTCCAGCCTG  
SEQ. ID. NO. 23 TGGAAACTCTATGCCACTGTGGGCCTGCTG

SEQ. ID. NO. 22 GGCATTGTTCTTGGCTGTTGTCTGTCTGTCC  
SEQ. ID. NO. 23 GTGGGGCATGGATGTCCTGACTCTTGGCCATC

SEQ. ID. NO. 22 TTTAACATCTACAACCTCCCACGTTTCGTTAT  
SEQ. ID. NO. 23 TGGCAGATTGTGGACCCCTTGCAACCGAACC

SEQ. ID. NO. 22 ATCCAGAACTCCCAGGCCCAACCTGAACAAT  
SEQ. ID. NO. 23 ATTGAGACTTTTGCCAAAGGAGGGAACCAAG

SEQ. ID. NO. 22 CTGACTGCTGTGGGCTGCTCACTGGGCACTG  
SEQ. ID. NO. 23 GAAGACATCGATGTCTCCATTCTGCCCCAG

*FIG. 6e.*

34/III

SEQ. ID. NO. 22 G C T G C T G T C T T C C C T C T C G G G C T G G A T G G T  
SEQ. ID. NO. 23 T T G G A G C A C T G C A G C T C C A A G A A G A T G A A T

SEQ. ID. NO. 22 T A C C A C A T A G G G A G A A G C C A G T T C C C G T T T  
SEQ. ID. NO. 23 A C G T G G C T T G G C A T T T T C T A T G G T T A C A A G

SEQ. ID. NO. 22 G T C T G C C A G G C C C G C C T T T G G C T C T T G G G C  
SEQ. ID. NO. 23 G G G C T G C T G C T G C T G C T G G G A A T C T T T C T T

SEQ. ID. NO. 22 T T G G G C T T T A G T C T G G G C T A T G G C T C T A T G  
SEQ. ID. NO. 23 G C T T A C G A A A C C A A G A G C G T G T C C A C T G A A

SEQ. ID. NO. 22 T T C A C C A A G A T C T G G T G G G T C C A C A C A G T C  
SEQ. ID. NO. 23 A A G A T C A A T G A C C A C A G G G C C G T G G G C A T G

SEQ. ID. NO. 22 T T C A C G A A G A A G G A G G A G A A G A A G G A G T G G  
SEQ. ID. NO. 23 G C T A T C T A C A A T G T C G C G G T C C T G T G T C T C

SEQ. ID. NO. 22 A G G A A G A C C C T A G A G C C C T G G A A A C T C T A T  
SEQ. ID. NO. 23 A T C A C T G C T C C T G T G A C C A T G A T C C T T T C C

SEQ. ID. NO. 22 G C C A C T G T G G G C C T G C T G G T G G G C A T G G A T  
SEQ. ID. NO. 23 A G T C A G C A G G A C G C A G C C T T T G C C T T T G C C

SEQ. ID. NO. 22 G T C C T G A C T C T T G C C A T C T G G C A G A T T G T G  
SEQ. ID. NO. 23 T C T C T G G C C A T C G T G T T C T C T T C C T A C A T C

SEQ. ID. NO. 22 G A C C C C T T G C A C C G A A C C A T T G A G A C T T T T  
SEQ. ID. NO. 23 A C T C T G G T T G T G C T C T T T G T G C C C A A G A T G

SEQ. ID. NO. 22 G C C A A G G A G G A A C C A A A G G A A G A C A T C G A T  
SEQ. ID. NO. 23 C G C A G G C T G A T C A C C C G A G G G G A A T G G C A G

SEQ. ID. NO. 22 G T C T C C A T T C T G C C C C A G T T G G A G C A C T G C  
SEQ. ID. NO. 23 T C T G A A A C G C A G G A C A C C A T G A A A A C A G G A

SEQ. ID. NO. 22 A G C T C C A A G A A G A T G A A T A C G T G G C T T G G C  
SEQ. ID. NO. 23 T C A T C C A C C A A C A A C A A C G A G G A A G A G A A G

FIG. 6f

35/III

SEQ. ID. NO. 22 A T T T T C T A T G G T T A C A A G G G G C T G C T G C T G  
SEQ. ID. NO. 23 T C C C G A C T G T T G G A G A A G G A A A A C C G A G A A

SEQ. ID. NO. 22 C T G C T G G G A A T C T T T C T T G C T T A C G A A A C C  
SEQ. ID. NO. 23 C T G G A A A A G A T C A T C G C T G A G A A A G A G G A G

SEQ. ID. NO. 22 A A G A G C G T G T C C A C T G A A A A G A T C A A T G A C  
SEQ. ID. NO. 23 C G C G T C T C T G A A C T G C G C C A T C A G C T C C A G

SEQ. ID. NO. 22 C A C A G G G C C G T G G G C A T G G C T A T C T A C A A T  
SEQ. ID. NO. 23 T C T C G G C A G C A A C T C C G C T C A C G G C G C C A C

SEQ. ID. NO. 22 G T C G C G G T C C T G T G T C T C A T C A C T G C T C C T  
SEQ. ID. NO. 23 C C C C C A A C A C C C C C A G A T C C C T C T G G G G G C

SEQ. ID. NO. 22 G T G A C C A T G A T C C T T T C C A G T C A G C A G G A C  
SEQ. ID. NO. 23 C T T C C C A G G G G A C C C T C T G A G C C C C C T G A C

SEQ. ID. NO. 22 G C A G C C T T T G C C T T T G C C T C T C T G G C C A T C  
SEQ. ID. NO. 23 C G G C T T A G C T G T G A T G G G A G T C G A G T A C A T

SEQ. ID. NO. 22 G T G T T C T C T T C C T A C A T C A C T C T G G T T G T G  
SEQ. ID. NO. 23 T T G C T T T A C A A G

SEQ. ID. NO. 22 C T C T T T G T G C C C A A G A T G C G C A G G C T G A T C  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 A C C C G A G G G G A A T G G C A G T C T G A A A C G C A G  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A C A C C A T G A A A A C A G G A T C A T C C A C C A A C  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 A A C A A C G A G G A A G A G A A G T C C C G A C T G T T G  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A G A A G G A A A A C C G A G A A C T G G A A A A G A T C  
SEQ. ID. NO. 23

FIG. 6g.

36/III

SEQ. ID. NO. 22 A T C G C T G A G A A A G A G G A G C G C G T C T C T G A A  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C T G C G C C A T C A G C T C C A G T C T C G G C A G C A A  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C T C C G C T C A C G G C G C C A C C C C C C A A C A C C C  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C C A G A T C C C T C T G G G G G C C T T C C C A G G G G A  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 C C C T C T G A G C C C C C T G A C C G G C T T A G C T G T  
SEQ. ID. NO. 23

SEQ. ID. NO. 22 G A T G G G A G T C G A G T A C A T T T G C T T T A C A A G  
SEQ. ID. NO. 23

*FIG. 6h.*

37/III

SEQ. ID. NO. 24 M L L L L L V P L F L R P L G A G G A Q T P N A T S E G C Q  
 SEQ. ID. NO. 25 M G P G G P C T P V G W P L P L L L V M A A G V A P V W A S

SEQ. ID. NO. 24 I I H P P W E G G I R Y R G L T R D Q V K A I N F L P V D Y  
 SEQ. ID. NO. 25 H S P H L P R P H P R V P P H P S S E R R A V Y I G A L F P

SEQ. ID. NO. 24 E I E Y V C R G E R E V V G P K V R K C L A N G S W T D M D  
 SEQ. ID. NO. 25 M S G G W P G G Q A C Q P A V E M A L E D V N S R R D I L P

SEQ. ID. NO. 24 T P S R C V R I C S K S Y L T L E N G K V F L T G G D L P A  
 SEQ. ID. NO. 25 D Y E L K L I H H D S K C D P G Q A T K Y L Y E L L Y N D P

SEQ. ID. NO. 24 L D G A R V E F R C D P D F H L V G S S R S V C S Q G Q W S  
 SEQ. ID. NO. 25 I K I I L M P G C S S V S T L V A E A A R M W N L I V L S Y

SEQ. ID. NO. 24 T P K P H C Q V N R T P H S E R R A V Y I G A L F P M S G G  
 SEQ. ID. NO. 25 G S S S P A L S N R Q R F P T F F R T H P S A T L H N P T R

SEQ. ID. NO. 24 W P G G Q A C Q P A V E M A L E D V N S R R D I L P D Y E L  
 SEQ. ID. NO. 25 V K L F E K W G W K K I A T I Q Q T T E V F T S T L D D L E

SEQ. ID. NO. 24 K L I H H D S K C D P G Q A T K Y L Y E L L Y N D P I K I I  
 SEQ. ID. NO. 25 E R V K E A G I E I T F R Q S F F S D P A V P V K N L K R Q

SEQ. ID. NO. 24 L M P G C S S V S T L V A E A A R M W N L I V L S Y G S S S  
 SEQ. ID. NO. 25 D A R I I V G L F Y E T E A R K V F C E V Y K E R L F G K K

SEQ. ID. NO. 24 P A L S N R Q R F P T F F R T H P S A T L H N P T R V K L F  
 SEQ. ID. NO. 25 Y V W F L I G W Y A D N W F K T Y D P S I N C T V E E M T E

SEQ. ID. NO. 24 E K W G W K K I A T I Q Q T T E V F T S T L D D L E E R V K  
 SEQ. ID. NO. 25 A V E G H I T T E I V M L N P A N T R S I S N M T S Q E F V

SEQ. ID. NO. 24 E A G I E I T F R Q S F F S D P A V P V K N L K R Q D A R I  
 SEQ. ID. NO. 25 E K L T K R L K R H P E E T G G F Q E A P L A Y D A I W A L

*FIG. 7a*

38/III

SEQ. ID. NO. 24 I V G L F Y E T E A R K V F C E V Y K E R L F G K K Y V W F  
 SEQ. ID. NO. 25 A L A L N K T S G G G G R S G V R L E D F N Y N N Q T I T D

SEQ. ID. NO. 24 L I G W Y A D N W F K T Y D P S I N C T V E E M T E A V E G  
 SEQ. ID. NO. 25 Q I Y R A M N S S S F E G V S G H V V F D A S G S R M A W T

SEQ. ID. NO. 24 H I T T E I V M L N P A N T R S I S N M T S Q E F V E K L T  
 SEQ. ID. NO. 25 L I E Q L Q G G S Y K K I G Y Y D S T K D D L S W S K T D K

SEQ. ID. NO. 24 K R L K R H P E E T G G F Q E A P L A Y D A I W A L A L A L  
 SEQ. ID. NO. 25 W I G G S P P A D Q I L V I K T F R F L S Q K L F I S V S V

SEQ. ID. NO. 24 N K T S G G G G R S G V R L E D F N Y N N Q T I T D Q I Y R  
 SEQ. ID. NO. 25 L S S L G I V L A V V C L S F N I Y N S H V R Y I O N S O P

SEQ. ID. NO. 24 A M N S S S F E G V S G H V V F D A S G S R M A W T L I E Q  
 SEQ. ID. NO. 25 N L N N L T A V G C S L A L A A V F P L G L D G Y H I G R S

SEQ. ID. NO. 24 L Q G G S Y K K I G Y Y D S T K D D L S W S K T D K W I G G  
 SEQ. ID. NO. 25 Q F P F V C Q A R L W L L G L G F S L G Y G S M F T K I W W

SEQ. ID. NO. 24 S P P A D Q I L V I K T F R F L S Q K L F I S V S V L S S L  
 SEQ. ID. NO. 25 V H T V F T K K E E K K E W R K T L E P W K L Y A T V G L L

SEQ. ID. NO. 24 G I V L A V V C L S F N I Y N S H V R Y I O N S Q P N L N N  
 SEQ. ID. NO. 25 V G M D V L T L A I W Q I V D P L H R T I E T F A K E E P K

SEQ. ID. NO. 24 L T A V G C S L A L A A V F P L G L D G Y H I G R S Q F P F  
 SEQ. ID. NO. 25 E D I D V S I L P Q L E H C S S K K M N T W L G I F Y G Y K

SEQ. ID. NO. 24 V C Q A R L W L L G L G F S L G Y G S M F T K I W W V H T V  
 SEQ. ID. NO. 25 G L L L L L G I F L A Y E T K S V S T E K I N D H R A V G M

SEQ. ID. NO. 24 F T K K E E K K E W R K T L E P W K L Y A T V G L L V G M D  
 SEQ. ID. NO. 25 A I Y N V A V L C L I T A P V T M I L S S Q Q D A A F A F A

SEQ. ID. NO. 24 V L T L A I W Q I V D P L H R T I E T F A K E E P K E D I D  
 SEQ. ID. NO. 25 S L A I V F S S Y I T L V V L F V P K M R R L I T R G E W O

FIG. 7b.

39/III

SEQ. ID. NO. 24 V S I L P Q L E H C S S K K M N T W L G I F Y G Y K G L L L  
SEQ. ID. NO. 25 S E T Q D T M K T G S S T N N N E E E K S R L L E K E N R E

SEQ. ID. NO. 24 L L G I F L A Y E T K S V S T E K I N D H R A V G M A I Y N  
SEQ. ID. NO. 25 L E K I I A E K E E R V S E L R H Q L Q S R Q Q L R S R R H

SEQ. ID. NO. 24 V A V L C L I T A P V T M I L S S Q O D A A F A F A S L A I  
SEQ. ID. NO. 25 P P T P P D P S G G L P R G P S E P P D R L S C D G S R V H

SEQ. ID. NO. 24 V F S S Y I T L V V L F V P K M R R L I T R G E W Q S E T Q  
SEQ. ID. NO. 25 L L Y K

SEQ. ID. NO. 24 D T M K T G S S T N N N E E E K S R L L E K E N R E L E K I  
SEQ. ID. NO. 25

SEQ. ID. NO. 24 I A E K E E R V S E L R H Q L Q S R Q Q L R S R R H P P T P  
SEQ. ID. NO. 25

SEQ. ID. NO. 24 P D P S G G L P R G P S E P P D R L S C D G S R V H L L Y K  
SEQ. ID. NO. 25

*FIG. 7c.*

40/III

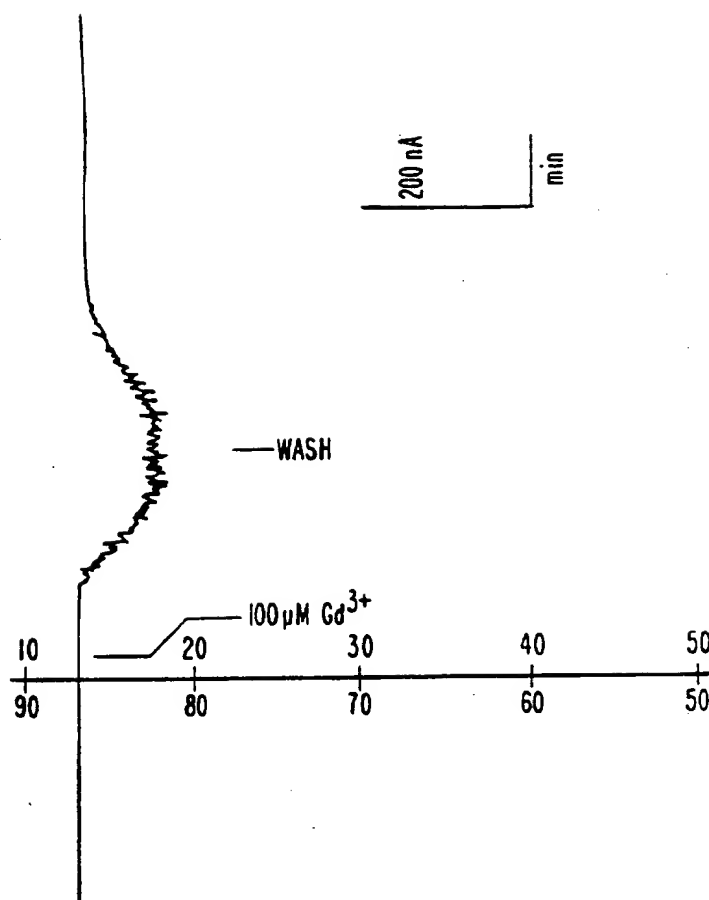


FIG. 8.



41/III

## ClustalW Formatted Alignments

SEQ. ID. NO. 38 A T G G T A T G C G A G G G A A A G C G A T C A G  
SEQ. ID. NO. 34 A T G G G A T C G C T G C T T G C G C T C C C G G  
SEQ. ID. NO. 30 A T G G C A T T T T A T A G C T G C T G C T G G G  
SEQ. ID. NO. 26 A T G G G A T C G C T G C T T G C G C T C C T G G

SEQ. ID. NO. 38 C C T C T T G C C C T T G T T T C T T C C T C T T  
SEQ. ID. NO. 34 C A C T G C T G C T G C T G T G G G G T G C T G T  
SEQ. ID. NO. 30 T C C T C T T G G C A C T C A C C T G G C A C A C  
SEQ. ID. NO. 26 C A C T G C T G C C G C T G T G G G G T G C T G T

SEQ. ID. NO. 38 G A C C G C C A A G T T C T A C T G G A T C C T C  
SEQ. ID. NO. 34 G G C T G A G G G C C C A G C C A A G A A G G T G  
SEQ. ID. NO. 30 C T C T G C C T A C G G G C C A G A C C A G C G A  
SEQ. ID. NO. 26 G G C T G A G G G C C C A G C C A A G A A G G T G

SEQ. ID. NO. 38 A C A A T G A T G C A A A G A A C T C A C A G C C  
SEQ. ID. NO. 34 C T G A C C C T G G A G G G A G A C T T G G T G C  
SEQ. ID. NO. 30 G C C C A A A A G A A A G G G G G A C A T T A T C C  
SEQ. ID. NO. 26 C T G A C C C T G G A G G G A G A C T T G G T G C

SEQ. ID. NO. 38 A G G A G T A T G C C C A T T C C A T A C G G G T  
SEQ. ID. NO. 34 T G G G T G G G C T G T T C C C A G T G C A C C A  
SEQ. ID. NO. 30 T T G G G G G G C T C T T T C C T A T T C A T T T  
SEQ. ID. NO. 26 T G G G T G G G C T G T T C C C A G T G C A C C A

SEQ. ID. NO. 38 G G A T G G G G A C A T T A T T T T G G G G G G T  
SEQ. ID. NO. 34 G A A G G G C G G C C C A G C A G A G G A C T G T  
SEQ. ID. NO. 30 T G G A G T A G C A G C T A A A G A T C A A G A T  
SEQ. ID. NO. 26 G A A G G G C G G C C C A G C A G A G G A C T G T

SEQ. ID. NO. 38 C T C T T C C C T G T C C A C G C A A A G G G A G  
SEQ. ID. NO. 34 G G T C C T G T C A A T G A G C A C C G T G G C A  
SEQ. ID. NO. 30 C T C A A A T C A A G G C C G G A G T C T G T G G  
SEQ. ID. NO. 26 G G T C C T G T C A A T G A G C A C C G T G G C A

SEQ. ID. NO. 38 A G A G A G G G G T G C C T T G T G G G G A G C T  
SEQ. ID. NO. 34 T C C A G C G C C T G G A G G C C A T G C T T T T  
SEQ. ID. NO. 30 A A T G T A T C A G G T A T A A T T T C C G T G G  
SEQ. ID. NO. 26 T C C A G C G C C T G G A G G C C A T G C T T T T

FIG. 9a.

42/III

SEQ. ID. NO. 38 G A A G A A G G A A A A G G G A T T C A C A G A  
SEQ. ID. NO. 34 T G C A C T G G A C C G C A T C A A C C G T G A C  
SEQ. ID. NO. 30 G T T T C G C T G G T T A C A G G C T A T G A T A  
SEQ. ID. NO. 26 T G C A C T G G A C C G C A T C A A C C G T G A C

SEQ. ID. NO. 38 C T G G A G G C C A T G C T T T A T G C A A T T G  
SEQ. ID. NO. 34 C C G C A C C T G C T G C C T G G C G T G C G C C  
SEQ. ID. NO. 30 T T T G C C A T A G A G G A G A T A A A C A G C A  
SEQ. ID. NO. 26 C C G C A C C T G C T G C C T G G C G T G C G C C

SEQ. ID. NO. 38 A C C A G A T T A A C A A G G A C C C T G A T C T  
SEQ. ID. NO. 34 T G G G T G C A C A C A T C C T C G A C A G T T G  
SEQ. ID. NO. 30 G C C C A G C C C T T C T T C C C A A C T T G A C  
SEQ. ID. NO. 26 T G G G T G C A C A C A T C C T C G A C A G T T G

SEQ. ID. NO. 38 C C T T T C C A A C A T C A C T C T G G G T G T C  
SEQ. ID. NO. 34 C T C C A A G G A C A C A C A T G C G C T G G A G  
SEQ. ID. NO. 30 G C T G G G A T A C A G G A T A T T T G A C A C T  
SEQ. ID. NO. 26 C T C C A A G G A C A C A C A T G C G C T G G A G

SEQ. ID. NO. 38 C G C A T C C T C G A C A C G T G C T C T A G G G  
SEQ. ID. NO. 34 C A G G C A C T G G A C T T T G T G C G T G C C T  
SEQ. ID. NO. 30 T G C A A C A C C G T T T T C T A A G G C C T T G G  
SEQ. ID. NO. 26 C A G G C A C T G G A C T T T G T G C G T G C C T

SEQ. ID. NO. 38 A C A C C T A T G C T T T G G A G C A G T C T C T  
SEQ. ID. NO. 34 C A C T C A G C C G T G G T G C T G A T G G C T C  
SEQ. ID. NO. 30 A A G C C A C C C T G A G T T T T G T T G C T C A  
SEQ. ID. NO. 26 C A C T C A G C C G T G G T G C T G A T G G A T C

SEQ. ID. NO. 38 A A C A T T C G T G C A G G C A T T A A T A G A G  
SEQ. ID. NO. 34 A C G C C A C A T C T G C C C C G A C G G C T C T  
SEQ. ID. NO. 30 A A A C A A A A T T G A T T C T T T G A A C C T T  
SEQ. ID. NO. 26 A C G C C A C A T C T G C C C C G A C G G C T C T

SEQ. ID. NO. 38 A A A G A T G C T T C G G A T G T G A A G T G T G  
SEQ. ID. NO. 34 T A T G C G A C C C A T G G T G A T G C T C C C A  
SEQ. ID. NO. 30 G A T G A G T T C T G C A A C T G C T C A G A G C  
SEQ. ID. NO. 26 T A T G C G A C C C A T G G T G A T G C T C C C A

*FIG. 9b.*

SUBSTITUTE SHEET (RULE 26)

43/III

SEQ. ID. NO. 38 C T A A T G G A G A T C C A C C C A T T T T C A C  
SEQ. ID. NO. 34 C T G C C A T C A C T G G T G T T A T T G G C G G  
SEQ. ID. NO. 30 A C A T T C C C T C T A C G A T T G C T G T G G T  
SEQ. ID. NO. 26 C T G C C A T C A C T G G T G T T A T T G G C G G

SEQ. ID. NO. 38 C A A G C C C G A C A A G A T T T C T G G C G T C  
SEQ. ID. NO. 34 T T C C T A C A G T G A T G T C T C C A T C C A G  
SEQ. ID. NO. 30 G G G A G C A A C T G G C T C A G G C G T C T C C  
SEQ. ID. NO. 26 T T C C T A C A G T G A T G T C T C C A T C C A G

SEQ. ID. NO. 38 A T A G G T G C T G C A G C A A G C T C C G T G T  
SEQ. ID. NO. 34 G T G G C C A A C C T C T T G A G G C T A T T T C  
SEQ. ID. NO. 30 A C G G C A G T G G C A A A T C T G C T G G G G C  
SEQ. ID. NO. 26 G T G G C C A A C C T C T T G A G G C T A T T T C

SEQ. ID. NO. 38 C C A T C A T G G T T G C T A A C A T T T T A A G  
SEQ. ID. NO. 34 A G A T C C C A C A G A T T A G C T A C G C C T C  
SEQ. ID. NO. 30 T C T T C T A C A T T C C C C A G G T C A G T T A  
SEQ. ID. NO. 26 A G A T C C C A C A G A T T A G C T A C G C C T C

SEQ. ID. NO. 38 A C T T T T T A A G A T A C C T C A A A T C A G C  
SEQ. ID. NO. 34 T A C C A G T G C C A A G C T G A G T G A C A A G  
SEQ. ID. NO. 30 T G C C T C C T C C A G C A G A C T C C T C A G C  
SEQ. ID. NO. 26 T A C C A G T G C C A A G C T G A G T G A C A A G

SEQ. ID. NO. 38 T A T G C A T C C A C A G C C C C A G A G C T A A  
SEQ. ID. NO. 34 T C C C G C T A T G A C T A C T T T G C C C G C A  
SEQ. ID. NO. 30 A A C A A G A A T C A A T T C A A G T C T T T C C  
SEQ. ID. NO. 26 T C C C G C T A T G A C T A C T T T G C C C G C A

SEQ. ID. NO. 38 G T G A T A A C A C C A G G T A T G A C T T T T T  
SEQ. ID. NO. 34 C A G T G C C T C C T G A C T T C T T C C A A G C  
SEQ. ID. NO. 30 T C C G A A C C A T C C C C A A T G A T G A G C A  
SEQ. ID. NO. 26 C A G T G C C T C C T G A C T T C T T C C A A G C

SEQ. ID. NO. 38 C T C T C G A G T G G T T C C G C C T G A C T C C  
SEQ. ID. NO. 34 C A A G G C C A T G G C T G A G A T T C T C C G C  
SEQ. ID. NO. 30 C C A G G C C A C T G C C A T G G C A G A C A T C  
SEQ. ID. NO. 26 C A A G G C C A T G G C T G A G A T T C T C C G C

*FIG. 9c.*

44/III

SEQ. ID. NO. 38 T A C C A A G C C C A A G C C A T G G T G G A C A  
SEQ. ID. NO. 34 T T C T T C A A C T G G A C C T A T G T G T C C A  
SEQ. ID. NO. 30 A T C G A G T A T T T C C G C T G G A A C T G G G  
SEQ. ID. NO. 26 T T C T T C A A C T G G A C C T A T G T G T C C A

SEQ. ID. NO. 38 T C G T G A C A G C A C T G G G A T G G A A T T A  
SEQ. ID. NO. 34 C T G T G G C G T C T G A G G G C G A C T A T G G  
SEQ. ID. NO. 30 T G G G C A C A A T T G C A G C T G A T G A C G A  
SEQ. ID. NO. 26 C T G A G G C C T C T G A G G G C G A C T A T G G

SEQ. ID. NO. 38 T G T T T C G A C A C T G G C T T C T G A G G G G  
SEQ. ID. NO. 34 C G A G A C A G G C A T T G A G G C C T T T G A C  
SEQ. ID. NO. 30 C T A T G G G C G G C C G G G A T T G A G A A A  
SEQ. ID. NO. 26 C G A G A C A G G C A T T G A G G C C T T T G A G

SEQ. ID. NO. 38 A A C T A T G G T G A G A G C G G T G T G G A G G  
SEQ. ID. NO. 34 C T A G A G G C T C G T G C C C G C A A C A T C T  
SEQ. ID. NO. 30 T T C C G A G A G G A A G C T G A G G A A A G G G  
SEQ. ID. NO. 26 C T A G A G G C T C G T G C C C G C A A C A T C T

SEQ. ID. NO. 38 C C T T C A C C C A G A T C T C G A G G G A G A T  
SEQ. ID. NO. 34 G T G T G G C C A C C T C G G A G A A A G T G G G  
SEQ. ID. NO. 30 A T A T C T G C A T C G A C T T C A G T G A A C T  
SEQ. ID. NO. 26 G T G T G G C C A C C T C G G A G A A A G T G G G

SEQ. ID. NO. 38 T G G T G G T G T T T G C A T T G C T C A G T C A  
SEQ. ID. NO. 34 C C G T G C C A T G A G C C G C G C G G C C T T T  
SEQ. ID. NO. 30 C A T C T C C C A G T A C T C T G A T G A G G A A  
SEQ. ID. NO. 26 C C G T G C C A T G A G C C G C G C G G C C T T T

SEQ. ID. NO. 38 C A G A A A A T C C C A C G T G A A C C A A G A C  
SEQ. ID. NO. 34 G A G G G T G T G G T G C G A G C C C T G C T G C  
SEQ. ID. NO. 30 G A G A T C C A G C A T G T G G T A G A G G T G A  
SEQ. ID. NO. 26 G A G G G T G T G G T G C G A G C C C T G C T G C

SEQ. ID. NO. 38 C T G G A G A A T T T G A A A A A A T T A T C A A  
SEQ. ID. NO. 34 A G A A G C C C A G T G C C C G C G T G G C T G T  
SEQ. ID. NO. 30 T T C A A A A T T C C A C G G C C A A A G T C A T  
SEQ. ID. NO. 26 A G A A G C C C A G T G C C C G C G T G G C T G T

*FIG. 9d.*

45/III

SEQ. ID. NO. 38 A C G C C T G C T A G A A A C A C C T A A T G C T  
SEQ. ID. NO. 34 C C T G T T C A C C C G T T C T G A G G A T G C C  
SEQ. ID. NO. 30 C G T G G T T T T C T C C A G T G G C C C A G A T  
SEQ. ID. NO. 26 C C T G T T C A C C C G T T C T G A G G A T G C C

SEQ. ID. NO. 38 C G A G C A G T G A T T A T G T T T G C C A A T G  
SEQ. ID. NO. 34 C G G G A G C T G C T T G C T G C C A G C C A G C  
SEQ. ID. NO. 30 C T T G A G C C C C T C A T C A A G G A G A T T G  
SEQ. ID. NO. 26 C G G G A G C T G C T T G C T G C C A G C C A G C

SEQ. ID. NO. 38 A G G A T G A C A T C A G G A G G A T A T T G G A  
SEQ. ID. NO. 34 G C C T C A A T G C C A G C T T C A C C T G G G T  
SEQ. ID. NO. 30 T C C G G C G C A A T A T C A C G G G C A A G A T  
SEQ. ID. NO. 26 G C C T C A A T G C C A G C T T C A C C T G G G T

SEQ. ID. NO. 38 A G C A G C A A A A A A A C T A A A C C A A A G T  
SEQ. ID. NO. 34 G G C C A G T G A T G G T T G G G G G G C C C T G  
SEQ. ID. NO. 30 C T G G C T G G C C A G C G A G G C C T G G G C C  
SEQ. ID. NO. 26 G G C C A G T G A T G G T T G G G G G G C C C T G

SEQ. ID. NO. 38 G G G C A T T T T C T C T G G A T T G G C T C A G  
SEQ. ID. NO. 34 G A G A G T G T G G T G G C A G G C A G T G A G G  
SEQ. ID. NO. 30 A G C T C C T C C C T G A T C G C C A T G C C T C  
SEQ. ID. NO. 26 G A G A G T G T G G T G G C A G G C A G T G A G G

SEQ. ID. NO. 38 A T A G T T G G G G A T C C A A A A T A G C A C C  
SEQ. ID. NO. 34 G G G C T G C T G A G G G T G C T A T C A C C A T  
SEQ. ID. NO. 30 A G T A C T T C C A C G T G G T T G G C G G C A C  
SEQ. ID. NO. 26 G G G C T G C T G A G G G T G C T A T C A C C A T

SEQ. ID. NO. 38 T G T C T A T C A G C A A G A G G A G A T T G C A  
SEQ. ID. NO. 34 C G A G C T G G C C T C C T A C C C C A T C A G T  
SEQ. ID. NO. 30 C A T T G G A T T C G C T C T G A A G G C T G G G  
SEQ. ID. NO. 26 C G A G C T G G C C T C C T A C C C C A T C A G T

SEQ. ID. NO. 38 G A A G G G G C T G T G A C A A T T T T G C C C A  
SEQ. ID. NO. 34 G A C T T T G C C T C C T A C T T C C A G A G C C  
SEQ. ID. NO. 30 C A G A T C C C A G G C T T C C G G G A A T T C C  
SEQ. ID. NO. 26 G A C T T T G C C T C C T A C T T C C A G A G C C

*FIG. 9e.*

SUBSTITUTE SHEET (RULE 26)

46/III

SEQ. ID. NO. 38 A A C G A G C A T C A A T T G A T G G A T T T G A  
SEQ. ID. NO. 34 T G G A C C C T T G G A A C A A C A G C C G G A A  
SEQ. ID. NO. 30 T G A A G A A G G T C C A T C C C A G G A A G T C  
SEQ. ID. NO. 26 T G G A C C C T T G G A A C A A C A G C C G G A A

SEQ. ID. NO. 38 T C G A T A C T T T A G A A G C C G A A C T C T T  
SEQ. ID. NO. 34 C C C C T G G T T C C G T G A A T T C T G G G A G  
SEQ. ID. NO. 30 T G T C C A C A A T G G T T T T G C C A A G G A G  
SEQ. ID. NO. 26 C C C C T G G T T C C G T G A A T T C T G G G A G

SEQ. ID. NO. 38 G C C A A T A A T C G A A G A A A T G T G T G G T  
SEQ. ID. NO. 34 C A G A G G T T C C G C T G C A G C T T C C G G C  
SEQ. ID. NO. 30 T T T T G G G A A G A A A C A T T T A A C T G C C  
SEQ. ID. NO. 26 C A G A G G T T C C G C T G C A G C T T C C G G C

SEQ. ID. NO. 38 T T G C A G A A T T C T G G G A G G A G A A T T T  
SEQ. ID. NO. 34 A G C G A G A C T G C G C A G C C C A C T C T C T  
SEQ. ID. NO. 30 A C C T C C A A G A A G G T G C A A A A G G A C C  
SEQ. ID. NO. 26 A G C G A G A C T G C G C A G C C C A C T C T C T

SEQ. ID. NO. 38 T G G C T G C A A G T T A G G A T C A C A T G G G  
SEQ. ID. NO. 34 C C G G G C T G T G C C C T T T G A G C A G G A G  
SEQ. ID. NO. 30 T T T A C C T G T G G A C A C C T T T C T G A G A  
SEQ. ID. NO. 26 C C G G G C T G T G C C C T T T G A A C A G G A G

SEQ. ID. NO. 38 A A A A G G A A C A G T C A T A T A A A G A A A T  
SEQ. ID. NO. 34 T C C A A G A T C A T G T T T G T G G T C A A T G  
SEQ. ID. NO. 30 G G T C A C G A A G A A A G T G G C G A C A G G T  
SEQ. ID. NO. 26 T C C A A G A T C A T G T T T G T G G T C A A T G

SEQ. ID. NO. 38 G C A C A G G G C T G G A G C G A A T T G C T C G  
SEQ. ID. NO. 34 C A G T G T A C G C C A T G G C C C A T G C G C T  
SEQ. ID. NO. 30 T T A G C A A C A G C T C G A C A G C C T T C C G  
SEQ. ID. NO. 26 C A G T G T A C G C C A T G G C C C A T G C G C T

SEQ. ID. NO. 38 G G A T T C A T C T T A T G A A C A G G A A G G A  
SEQ. ID. NO. 34 C C A C A A C A T G C A C C G T G C C C T C T G C  
SEQ. ID. NO. 30 A C C C C T C T G T A C A G G G G A T G A G A A C  
SEQ. ID. NO. 26 C C A C A A C A T G C A C C G T G C C C T C T G C

*FIG. 9f*

SUBSTITUTE SHEET (RULE 26)

47/III

SEQ. ID. NO. 38 A A G G T C C A A T T T G T A A T T G A T G C T G  
SEQ. ID. NO. 34 C C C A A C A C C A C C C G G C T C T G T G A C G  
SEQ. ID. NO. 30 A T C A G C A G T G T C G A G A C C C C T T A C A  
SEQ. ID. NO. 26 C C C A A C A C C A C C C G G C T C T G T G A C G

SEQ. ID. NO. 38 T A T A T T C C A T G G C T T A C G C C C T G C A  
SEQ. ID. NO. 34 C G A T G C G G C C A G T T A A C G G G C G C C G  
SEQ. ID. NO. 30 T A G A T T A C A C G C A T T T A C G G A T A T C  
SEQ. ID. NO. 26 C G A T G C G G C C A G T T A A C G G G C G C C G

SEQ. ID. NO. 38 C A A T A T G C A C A A A G A T C T C T G C C C T  
SEQ. ID. NO. 34 C C T C T A C A A G G A C T T T G T G C T C A A C  
SEQ. ID. NO. 30 C T A C A A T G T G T A C T T A G C A G T C T A C  
SEQ. ID. NO. 26 C C T C T A C A A G G A C T T T G T G C T C A A C

SEQ. ID. NO. 38 G G A T A C A T T G G C C T T T G T C C A C G A A  
SEQ. ID. NO. 34 G T C A A G T T T T G A T G C C C C C T T T C G C C  
SEQ. ID. NO. 30 T C C A T T G C C C A C G C C T T G C A A G A T A  
SEQ. ID. NO. 26 G T C A A G T T T T G A T G C C C C C T T T C G C C

SEQ. ID. NO. 38 T G A G T A C C A T T G A T G G G A A A G A G C T  
SEQ. ID. NO. 34 C A G C T G A C A C C C A C A A T G A G G T C C G  
SEQ. ID. NO. 30 T A T A T A C C T G C T T A C C T G G G A G A G G  
SEQ. ID. NO. 26 C A G C T G A C A C C C A C A A T G A G G T C C G

SEQ. ID. NO. 38 A C T T G G T T A T A T T C G G G C T G T A A A T  
SEQ. ID. NO. 34 C T T T G A C C G C T T T G G T G A T G G T A T T  
SEQ. ID. NO. 30 G C T C T T C A C C A A T G G C T C C T G T G C A  
SEQ. ID. NO. 26 C T T T G A C C G C T T T G G T G A T G G T A T T

SEQ. ID. NO. 38 T T T A A T G G C A G T G C T G G C A C T C C T G  
SEQ. ID. NO. 34 G G C C G C T A C A A C A T C T T C A C C T A T C  
SEQ. ID. NO. 30 G A C A T C A A G A A A G T T G A G G C G T G G C  
SEQ. ID. NO. 26 G G C C G C T A C A A C A T C T T C A C C T A T C

SEQ. ID. NO. 38 T C A C T T T T A A T G A A A A C G G A G A T G C  
SEQ. ID. NO. 34 T G C G T G C A G G C A G T G G G C G C T A T C G  
SEQ. ID. NO. 30 A G G T C C T G A A G C A C C T A C G G C A T C T  
SEQ. ID. NO. 26 T G C G T G C A G G C A G T G G G C G C T A T C G

*FIG. 9g.*

48/III

SEQ. ID. NO. 38 T C C T G G A C G T T A T G A T A T C T T C C A G  
SEQ. ID. NO. 34 C T A C C A G A A G G T G G G C T A C T G G G C A  
SEQ. ID. NO. 30 A A A C T T T A C A A A C A A T A T G G G G G A G  
SEQ. ID. NO. 26 C T A C C A G A A G G T G G G C T A C T G G G C A

SEQ. ID. NO. 38 T A T C A A A T A A C C A A C A A A A G C A C A G  
SEQ. ID. NO. 34 G A A G G C T T T G A C T C T G G A C A C C A G C C  
SEQ. ID. NO. 30 C A G G T G A C C T T T G A T G A G T G T G G T G  
SEQ. ID. NO. 26 G A A G G C T T G A C T C T G G A C A C C A G C C

SEQ. ID. NO. 38 A G T A C A A A G T C A T C G G C C A C T G G A C  
SEQ. ID. NO. 34 T C A T C C C A T G G G C C T C A C C C T C A G C  
SEQ. ID. NO. 30 A C C T G G T G G G G A A C T A T T C C A T C A T  
SEQ. ID. NO. 26 T C A T C C C A T G G G C C T C A C C G T C A G C

SEQ. ID. NO. 38 C A A T C A G C T T C A T C T A A A A G T G G A A  
SEQ. ID. NO. 34 C G G C C C C C T G C C C G C C T C T C G C T G C  
SEQ. ID. NO. 30 C A A C T G G C A C C T C T C C C C A G A G G A T  
SEQ. ID. NO. 26 C G G C C C C C T G G C C G C C T C T C G C T G C

SEQ. ID. NO. 38 G A C A T G C A G T G G G C T C A T A G A G A A C  
SEQ. ID. NO. 34 A G T G A G C C C T G C C T C C A G A A T G A G G  
SEQ. ID. NO. 30 G G C T C C A T C G T G T T T A A G G A A G T C G  
SEQ. ID. NO. 26 A G T G A G C C C T G C C T C C A G A A T G A G G

SEQ. ID. NO. 38 A T A C T C A C C C G G C G T C T G T C T G C A G  
SEQ. ID. NO. 34 T G A A G A G T G T G C A G C C G G G C G A A G T  
SEQ. ID. NO. 30 G G T A T T A C A A C G T C T A T G C C A A G A A  
SEQ. ID. NO. 26 T G A A G A G T G T G C A G C C G G G C G A A G T

SEQ. ID. NO. 38 C C T G C C G T G T A A G C C A G G G G A G A G G  
SEQ. ID. NO. 34 C T G C T G C T G G C T C T G C A T T C C G T G C  
SEQ. ID. NO. 30 G G G A G A A A G A C T C T T C A T C A A C G A G  
SEQ. ID. NO. 26 C T G C T G C T G G C T C T G C A T T C C G T G C

SEQ. ID. NO. 38 A A G A A A A C G G T G A A A G G G G T C C C T T  
SEQ. ID. NO. 34 C A G C C C T A T G A G T A C C G A T T G G A C G  
SEQ. ID. NO. 30 G A G A A A A T C C T G T G G A G T G G G T T C T  
SEQ. ID. NO. 26 C A G C C C T A T G A G T A C C G A T T G G A C G

*FIG. 9h.*

SUBSTITUTE SHEET (RULE 26)



49/III

SEQ. ID. NO. 38 G C T G C T G G C A C T G T G A A C G C T G T G A  
SEQ. ID. NO. 34 A A T T C A C T T G C G C T G A T T G T G G C C T  
SEQ. ID. NO. 30 C C A G G G A G G T G C C C T T C T C C A A C T G  
SEQ. ID. NO. 26 A A T T C A C T T G C G C T G A T T G T G G C C T

SEQ. ID. NO. 38 A G G T T A C A A C T A C C A G G T G G A T G A G  
SEQ. ID. NO. 34 G G G C T A C T G G C C C A A T G C C A G C C T G  
SEQ. ID. NO. 30 C A G C C G A G A C T G C C T G G C A G G G A C C  
SEQ. ID. NO. 26 G G G C T A C T G G C C C A A T G C C A G C C T G

SEQ. ID. NO. 38 C T G T C C T G T G A A C T T T G C C C T C T G G  
SEQ. ID. NO. 34 A C T G G C T G C T T C G A A C T G C C C C A G G  
SEQ. ID. NO. 30 A G G A A A G G G A T C A T T G A G G G G G A G C  
SEQ. ID. NO. 26 A C T G G C T G C T T C G A A C T G C C C C A G G

SEQ. ID. NO. 38 A T C A G A G A C C C A A C A T G A A C C G C A C  
SEQ. ID. NO. 34 A G T A C A T C C G C T G G G G C G A T G C C T G  
SEQ. ID. NO. 30 C C A C C T G C T G C T T T G A G T G T G T G G A  
SEQ. ID. NO. 26 A G T A C A T C C G C T G G G G C G A T G C C T G

SEQ. ID. NO. 38 A G G C T G C C A G C T T A T C C C C A T C A T C  
SEQ. ID. NO. 34 G G C T G T G G G A C C T G T C A C C A T C G C C  
SEQ. ID. NO. 30 G T G T C C T G A T G G G G A G T A T A G T G A T  
SEQ. ID. NO. 26 G G C T G T G G G A C C T G T C A C C A T C G C C

SEQ. ID. NO. 38 A A A T T G G A G T G G C A T T C T C C C T G G G  
SEQ. ID. NO. 34 T G C C T C G G T G C C C T G G C C A C C C T C T  
SEQ. ID. NO. 30 G A G A C A G A T G C C A G T G C C T G T A A C A  
SEQ. ID. NO. 26 T G C C T C G G T G C C C T G G C C A C C C T G T

SEQ. ID. NO. 38 C T G T G G T G C C T G T G T T T G T T G C A A T  
SEQ. ID. NO. 34 T T G T G C T G G G T G T C T T T G T G C G G C A  
SEQ. ID. NO. 30 A G T G C C C A G A T G A C T T C T G G T C C A A  
SEQ. ID. NO. 26 T T G T G C T G G G T G T C T T T G T G C G G C A

SEQ. ID. NO. 38 A T T G G G A A T C A T C G C C A C C A C C T T T  
SEQ. ID. NO. 34 C A A T G C C A C A C C A G T G G T C A A G G C C  
SEQ. ID. NO. 30 T G A G A A C C A C A C C T C C T G C T T C G A A  
SEQ. ID. NO. 26 C A A T G C C A C A C C A G T G G T C A A G G C C

*FIG. 9i.*

SUBSTITUTE SHEET (RULE 26)

50/III

SEQ. ID. NO. 38 GTGATCGTGACCTTTGTCCGCTATA  
SEQ. ID. NO. 34 TCAGGTCGGGAGCTCTGCTACATCC  
SEQ. ID. NO. 30 CTGCCCCAGGAGTACATCCGCTGGG  
SEQ. ID. NO. 26 TCAGGTCGGGAGCTCTGCTACATCC

SEQ. ID. NO. 38 ATGACACACCTATCGTGAGGGCTTC  
SEQ. ID. NO. 34 TGCTGGGTGGGTGTCCTCCTGCTA  
SEQ. ID. NO. 30 GCGATGCCCTGGGGCTGTGGGACCTGT  
SEQ. ID. NO. 26 TGCTGGGTGGGTGTCCTCCTGCTA

SEQ. ID. NO. 38 AGGACGCGAACTTAGTTACGTGCTC  
SEQ. ID. NO. 34 CTGCATGACCTTTCATCTTTCATTGCC  
SEQ. ID. NO. 30 CACCATCGCCTGCTCCTCGGTGCCCTG  
SEQ. ID. NO. 26 CTGCATGACCTTTCATCTTTCATTGCC

SEQ. ID. NO. 38 CTAACGGGGATTTTTCTCTGTATT  
SEQ. ID. NO. 34 AAGCCATCCACGGGCAGTGTGTACCT  
SEQ. ID. NO. 30 GCCACCCTGTTTTGTGCTGGGGTGTCT  
SEQ. ID. NO. 26 AAGCCATCCACGGGCAGTGTGTACCT

SEQ. ID. NO. 38 CAATCACGTTTTTTAATGATTGACAGC  
SEQ. ID. NO. 34 TACGGCGTCTTTGGTTTGGGGCACTGC  
SEQ. ID. NO. 30 TTGTGCGGGCACAATGCCACACCAGT  
SEQ. ID. NO. 26 TACGGCGTCTTTGGTTTGGGGCACTGC

SEQ. ID. NO. 38 ACCAGATACAAATCATATGCTCCTTTC  
SEQ. ID. NO. 34 CTTCTCTGTCTGTCTACTCAGCCCTG  
SEQ. ID. NO. 30 GGTCAAGGCCCTCAGGTGCGGGAGCTC  
SEQ. ID. NO. 26 CTTCTCTGTCTGTCTACTCAGCCCTG

SEQ. ID. NO. 38 CGACGGGTCTTTCCTAGGACTTTGGCA  
SEQ. ID. NO. 34 CTCACCAAGACCAACCGCATTTGCAC  
SEQ. ID. NO. 30 TGCTACATCCTGCTGGGTGGTGTCT  
SEQ. ID. NO. 26 CTCACCAAGACCAACCGCATTTGCAC

SEQ. ID. NO. 38 TGTGTTTTCAGCTATGACAGCCCTTCT  
SEQ. ID. NO. 34 GCATCTTTCGGGTGGGGGCCCGGGAGGG  
SEQ. ID. NO. 30 TCCTCTGCTACTGCATGACCTTTCAT  
SEQ. ID. NO. 26 GCATCTTTCGGGTGGGGGCCCGGGAGGG

FIG. 9j.

SUBSTITUTE SHEET (RULE 26)

51/III

SEQ. ID. NO. 38 G A C C A A A A C A A A C C G T A T C C A C C G A  
SEQ. ID. NO. 34 T G C C C A G C G G C C A C G C T T C A T C A G T  
SEQ. ID. NO. 30 C T T C A T T G C C A A G C C A T C C A C G G C A  
SEQ. ID. NO. 26 T G C C C A G C G G C C A C G C T T C A T C A G T

SEQ. ID. NO. 38 A T A T T T G A G C A G G G G A A G A A A T C T G  
SEQ. ID. NO. 34 C C T G C C T C A C A G G T G G C C A T C T G C C  
SEQ. ID. NO. 30 G T G T G T A C C T T A C G G C G T C T T G G T T  
SEQ. ID. NO. 26 C C T G C C T C A C A G G T G G C C A T C T G C C

SEQ. ID. NO. 38 T C A C A G C G C C C A A G T T C A T T A G T C C  
SEQ. ID. NO. 34 T G G C A C T T A T C T C G G G C C A G C T G C T  
SEQ. ID. NO. 30 T G G G C A C T G C C T T C T C T G T C T G C T A  
SEQ. ID. NO. 26 T G G C A C T T A T C T C G G G C C A G C T G C T

SEQ. ID. NO. 38 A G C A T C T C A G C T G G T G A T C A C C T T C  
SEQ. ID. NO. 34 C A T C G T G G T C G C C T G G C T G G T G G T G  
SEQ. ID. NO. 30 C T C A G C C C T G C T C A C C A A G A C C A A C  
SEQ. ID. NO. 26 C A T C G T G G T C G C C T G G C T G G T G G T G

SEQ. ID. NO. 38 A G C C T C A T C T C C G T C C A G C T C C T T G  
SEQ. ID. NO. 34 G A G G C A C C G G G C A C A G G C A A G G A G A  
SEQ. ID. NO. 30 C G C A T T G C A C G C A T C T T C G G T G G G G  
SEQ. ID. NO. 26 G A G G C A C C G G G C A C A G G C A A G G A G A

SEQ. ID. NO. 38 G A G T G T T T G T C T G G T T T G T T G T G G A  
SEQ. ID. NO. 34 C A G C C C C C G A A C G G C G G G A G G T G G T  
SEQ. ID. NO. 30 C C C G G G A G G G T G C C C A G C G G C C A C G  
SEQ. ID. NO. 26 C A G C C C C C G A A C G G C G G G A G G T G G T

SEQ. ID. NO. 38 T C C C C C C A C A T C A T C A T T G A C T A T  
SEQ. ID. NO. 34 G A C A C T G C G C T G C A A C C A C C G C G A T  
SEQ. ID. NO. 30 C T T C A T C A G T C C T G C C T C A C A G G T G  
SEQ. ID. NO. 26 G A C A C T G C G C T G C A A C C A C C G C G A T

SEQ. ID. NO. 38 G G A G A G C A G C G G A C A C T A G A T C C A G  
SEQ. ID. NO. 34 G C A A G T A T G T T G G G C T C G C T G G C C T  
SEQ. ID. NO. 30 G C C A T C T G C C T G G C A C T T A T C T C G G  
SEQ. ID. NO. 26 G C A A G T A T G T T G G G C T C G C T G G C C T

FIG. 9k.

SUBSTITUTE SHEET (RULE 26)

52/III

SEQ. ID. NO. 38 A G A A G G C C A G G G G A G T G C T C A A G T G  
SEQ. ID. NO. 34 A C A A T G T G C T C C T C A T C G C G C T C T G  
SEQ. ID. NO. 30 G C C A G C T G C T C A T C G T G G T C G C C T G  
SEQ. ID. NO. 26 A C A A T G T G C T C C T C A T C G C G C T C T G

SEQ. ID. NO. 38 T G A C A T T T C T G A T C T C T C A C T C A T T  
SEQ. ID. NO. 34 C A C G C T T T A T G C C T T C A A G A C T C G C  
SEQ. ID. NO. 30 G C T G G T G G T G G A G G C A C C G G G C A C A  
SEQ. ID. NO. 26 C A C G C T T T A T G C C T T C A A T A C T C G C

SEQ. ID. NO. 38 T G T T C A C T T G G A T A C A G T A T C C T C T  
SEQ. ID. NO. 34 A A G T G C C C C G A A A A C T T C A A C G A G G  
SEQ. ID. NO. 30 G G C A A G G A G A C A G C C C C C G A A C G G C  
SEQ. ID. NO. 26 A A G T G C C C C G A A A A C T T C A A C G A G G

SEQ. ID. NO. 38 T G A T G G T C A C T T G T A C T G T T T A T G C  
SEQ. ID. NO. 34 C C A A G T T C A T T G G C T T C A C C A T G T A  
SEQ. ID. NO. 30 G G G A G G T G G T G A C A C T G C G C T G C A A  
SEQ. ID. NO. 26 C C A A G T T C A T T G G C T T C A C C A T G T A

SEQ. ID. NO. 38 C A T T A A A A C G A G A G G T G T C C C A G A G  
SEQ. ID. NO. 34 C A C C A C C T G C A T C A T C T G G C T G G C A  
SEQ. ID. NO. 30 C C A C C G C G A T G C A A G T A T G T T G G G C  
SEQ. ID. NO. 26 C A C C A C C T G C A T C A T C T G G C T G G C A

SEQ. ID. NO. 38 A C T T T C A A T G A A G C C A A A C C T A T T G  
SEQ. ID. NO. 34 T T C C T G C C C A T C T T C T A T G T C A C C T  
SEQ. ID. NO. 30 T C G C T G G C C T A C A A T G T G C T C C T C A  
SEQ. ID. NO. 26 T T G T T G C C C A T C T T C T A T G T C A C C T

SEQ. ID. NO. 38 G A T T T A C C A T G T A T A C C A C C C T G C A T  
SEQ. ID. NO. 34 C C A G T G A C T A C C G G G T A C A G A C C A C  
SEQ. ID. NO. 30 T C G C G C T C T G C A C G C T T T A T G C C T T  
SEQ. ID. NO. 26 C C A G T G A C T A C C G G G T A C A G A C C A C

SEQ. ID. NO. 38 C A T T T G G T T A G C T T T C A T C C C C A T C  
SEQ. ID. NO. 34 C A C C A T G T G C G T G T C A G T C A G C C T C  
SEQ. ID. NO. 30 C A A T A C T C G C A A G T G C C C C G A A A A C  
SEQ. ID. NO. 26 C A C C A T G T G C G T G T C A G T C A G C C T C

FIG. 9L.

SUBSTITUTE SHEET (RULE 26)

53/III

SEQ. ID. NO. 38 T T T T T T G G T A C A G C C C A G T C A G C A G  
SEQ. ID. NO. 34 A G C G G C T C C G T G G T G C T T G G C T G C C  
SEQ. ID. NO. 30 T T C A A C G A G G C C A A G T T C A T T G G C T  
SEQ. ID. NO. 26 A G C G G C T C C G T G G T G C T T G G C T G C C

SEQ. ID. NO. 38 A A A A G A T G T A C A T C C A G A C A A C A A C  
SEQ. ID. NO. 34 T C T T T G C G C C C A A G C T G C A C A T C A T  
SEQ. ID. NO. 30 T C A C C A T G T A C A C C A C C T G C A T C A T  
SEQ. ID. NO. 26 T C T T T G C G C C C A A G C T G C A C A T C A T

SEQ. ID. NO. 38 A C T T A C T G T C T C C A T G A G T T T A A G T  
SEQ. ID. NO. 34 C C T C T T C C A G C C G C A G A A G A A C A C C  
SEQ. ID. NO. 30 C T G G C T G G C A T T G T T G C C C A T C T T C  
SEQ. ID. NO. 26 C C T C T T C C A G C C G C A G A A G A A C G T G

SEQ. ID. NO. 38 G C T T C A G T A T C T C T G G G C A T G C T C T  
SEQ. ID. NO. 34 A T C G A G G A G G T G C G T T G C A G C A C C G  
SEQ. ID. NO. 30 T A T G T C A C C T C C A G T G A C T A C C G G G  
SEQ. ID. NO. 26 G T T A G C C A C C G G G C A C C C A C C A G C C

SEQ. ID. NO. 38 A T A T G C C C A A G G T T T A T A T T A T A A T  
SEQ. ID. NO. 34 C A G C T C A C G C T T T C A A G G T G G C T G C  
SEQ. ID. NO. 30 T A C A G A C C A C C A C C A T G T G C G T G T C  
SEQ. ID. NO. 26 G C T T T G G C A G T G C T G C T G C C A G G G C

SEQ. ID. NO. 38 T T T T C A T C C A G A A C A G A A T A C C A T C  
SEQ. ID. NO. 34 C C G G G C C A C G C T G C G C C G C A G C A A C  
SEQ. ID. NO. 30 A G T C A G C C T C A G C G G C T C C G T G G T G  
SEQ. ID. NO. 26 C A G C T C C A G C C T T G G C C A A G G G T C T

SEQ. ID. NO. 38 G A G G A G G T G C G T T G C A G C A C C G C A G  
SEQ. ID. NO. 34 G T C T C C C G C A A G C G G T C C A G C A G C C  
SEQ. ID. NO. 30 C T T G G C T G C C T C T T T G C G C C C A A G C  
SEQ. ID. NO. 26 G G C T C C C A G T T T G T C C C C A C T G T T T

SEQ. ID. NO. 38 C T C A C G C T T T C A A G G T G G C T G C C C G  
SEQ. ID. NO. 34 T T G G A G G C T C C A C G G G A T C C A C C C C  
SEQ. ID. NO. 30 T G C A C A T C A T C C T C T T C C A G C C G C A  
SEQ. ID. NO. 26 G C A A T G G C C G T G A G G T G G T G G A C T C

*FIG. 9m.*

54/III

SEQ. ID. NO. 38 G G C C A C G C T G C G C C G C A G C A A C G T C  
SEQ. ID. NO. 34 C T C C T C C T C C A T C A G C A G C A A G A G C  
SEQ. ID. NO. 30 G A A G A A C G T G G T T A G C C A C C G G G C A  
SEQ. ID. NO. 26 G A C A A C G T C A T C G C T T

SEQ. ID. NO. 38 T C C C G C A A G C G G T C C A G C A G C C T T G  
SEQ. ID. NO. 34 A A C A G C G A A G A C C C A T T C C C A C A G C  
SEQ. ID. NO. 30 C C C A C C A G C C G C T T T G G C A G T G C T G  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G A G G C T C C A C G G G A T C C A C C C C C T C  
SEQ. ID. NO. 34 C C G A G A G G C A G A A G C A G C A G C A G C C  
SEQ. ID. NO. 30 C T G C C A G G G C C A G C T C C A G C C T T G G  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C T C C T C C A T C A G C A G C A A G A G C A A C  
SEQ. ID. NO. 34 G C T G G C C C T A A C C C A G C A A G A G C A G  
SEQ. ID. NO. 30 C C A A G G G T C T G G C T C C C A G T T T G T C  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G C G A A G A C C C A T T C C C A C A G C C C G  
SEQ. ID. NO. 34 C A G C A G C A G C C C C T G A C C C T C C C A C  
SEQ. ID. NO. 30 C C C A C T G T T T G C A A T G G C C G T G A G G  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G A G G C A G A A G C A G C A G C A G C C G C T  
SEQ. ID. NO. 34 A G C A G C A A C G A T C T C A G C A G C A G C C  
SEQ. ID. NO. 30 T G G T G G A C T C G A C A A C G T C A T C G C T  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G G C C C T A A C C C A G C A A G A G C A G C A G  
SEQ. ID. NO. 34 C A G A T G C A A G C A G A A G G T C A T C T T T  
SEQ. ID. NO. 30 T  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A G C A G C C C C T G A C C C T C C C A C A G C  
SEQ. ID. NO. 34 G G C A G C G G C A C G G T C A C C T T C T C A C  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

*FIG. 9n.*

55/III

SEQ. ID. NO. 38 A G C A A C G A T C T C A G C A G C A G C C C A G  
SEQ. ID. NO. 34 T G A G C T T T G A T G A G C C T C A G A A G A A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A T G C A A G C A G A A G G T C A T C T T T G G C  
SEQ. ID. NO. 34 C G C C A T G G C C C A C G G G A A T T C T A C G  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G C G G C A C G G T C A C C T T C T C A C T G A  
SEQ. ID. NO. 34 C A C C A G A A C T C C C T G G A G G C C C A G A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C T T T G A T G A G C C T C A G A A G A A C G C  
SEQ. ID. NO. 34 A A A G C A G C G A T A C G C T G A C C C G A C A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A T G G C C C A C G G G A A T T C T A C G C A C  
SEQ. ID. NO. 34 C C A G C C A T T A C T C C C G C T G C A G T G C  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A G A A C T C C C T G G A G G C C C A G A A A A  
SEQ. ID. NO. 34 G G G G A A A C G G A C T T A G A T C T G A C C G  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C A G C G A T A C G C T G A C C C G A C A C C A  
SEQ. ID. NO. 34 T C C A G G A A A C A G G T C T G C A A G G A C C  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G C C A T T A C T C C C G C T G C A G T G C G G G  
SEQ. ID. NO. 34 T G T G G G T G G A G A C C A G C G G C C A G A G  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

*FIG. 90.*

SUBSTITUTE SHEET (RULE 26)

56/III

SEQ. ID. NO. 38 G A A A C G G A C T T A G A T C T G A C C G T C C  
SEQ. ID. NO. 34 G T G G A G G A C C C T G A A G A G T T G T C C C  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A G G A A A C A G G T C T G C A A G G A C C T G T  
SEQ. ID. NO. 34 C A G C A C T T G T A G T G T C C A G T T C A C A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G G G T G G A G A C C A G C G G C C A G A G G T G  
SEQ. ID. NO. 34 G A G C T T T G T C A T C A G T G G T G G A G G C  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 G A G G A C C C T G A A G A G T T G T C C C C A G  
SEQ. ID. NO. 34 A G C A C T G T T A C A G A A A A C G T A G T G A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A C T T G T A G T G T C C A G T T C A C A G A G  
SEQ. ID. NO. 34 A T T C A  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C T T T G T C A T C A G T G G T G G A G G C A G C  
SEQ. ID. NO. 34  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 A C T G T T A C A G A A A A C G T A G T G A A T T  
SEQ. ID. NO. 34  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

SEQ. ID. NO. 38 C A  
SEQ. ID. NO. 34  
SEQ. ID. NO. 30  
SEQ. ID. NO. 26

*FIG. 9p.*

SUBSTITUTE SHEET (RULE 26)



57/III

## ClustalW Formatted Alignments

SEQ. ID. NO. 39 M V C E G K R S A S C P C F F L L T A K F Y W I L  
 SEQ. ID. NO. 35 M G S L L A L P A L L L L W G A V A E G P A K K V  
 SEQ. ID. NO. 31 M A F Y S C C W V L L A L T W H T S A Y G P D Q R  
 SEQ. ID. NO. 27 M G S L L A L L A L L P L W G A V A E G P A K K V

SEQ. ID. NO. 39 T M M Q R T H S Q E Y A H S I R V D G D I I L G G  
 SEQ. ID. NO. 35 L T L E G D L V L G G L F P V H Q K G G P A E D C  
 SEQ. ID. NO. 31 A Q K K G D I I L G G L F P I H F G V A A K D Q D  
 SEQ. ID. NO. 27 L T L E G D L V L G G L F P V H Q K G G P A E D C

SEQ. ID. NO. 39 L F P V H A K G E R G V P C G E L K K E K G I H R  
 SEQ. ID. NO. 35 G P V N E H R G I Q R L E A M L F A L D R I N R D  
 SEQ. ID. NO. 31 L K S R P E S V E C I R Y N F R G F R W L Q A M I  
 SEQ. ID. NO. 27 G P V N E H R G I Q R L E A M L F A L D R I N R D

SEQ. ID. NO. 39 L E A M L Y A I D Q I N K D P D L L S N I T L G V  
 SEQ. ID. NO. 35 P H L L P G V R L G A H I L D S C S K D T H A L E  
 SEQ. ID. NO. 31 F A I E E I N S S P A L L P N L T L G Y R I F D T  
 SEQ. ID. NO. 27 P H L L P G V R L G A H I L D S C S K D T H A L E

SEQ. ID. NO. 39 R I L D T C S R D T Y A L E Q S L T F V Q A L I E  
 SEQ. ID. NO. 35 Q A L D F V R A S L S R G A D G S R H I C P D G S  
 SEQ. ID. NO. 31 C N T V S K A L E A T L S F V A Q N K I D S L N L  
 SEQ. ID. NO. 27 Q A L D F V R A S L S R G A D G S R H I C P D G S

SEQ. ID. NO. 39 K D A S D V K C A N G D P P I F T K P D K I S G V  
 SEQ. ID. NO. 35 Y A T H G D A P T A I T G V I G G S Y S D V S I Q  
 SEQ. ID. NO. 31 D E F C N C S E H I P S T I A V V G A T G S G V S  
 SEQ. ID. NO. 27 Y A T H G D A P T A I T G V I G G S Y S D V S I Q

SEQ. ID. NO. 39 I G A A A S S V S I M V A N I L R L F K I P Q I S  
 SEQ. ID. NO. 35 V A N L L R L F Q I P Q I S Y A S T S A K L S D K  
 SEQ. ID. NO. 31 T A V A N L L G L F Y I P Q V S Y A S S S R L L S  
 SEQ. ID. NO. 27 V A N L L R L F Q I P Q I S Y A S T S A K L S D K

SEQ. ID. NO. 39 Y A S T A P E L S D N T R Y D F F S R V V P P D S  
 SEQ. ID. NO. 35 S R Y D Y F A R T V P P D F F Q A K A M A E I L R  
 SEQ. ID. NO. 31 N K N Q F K S F L R T I P N D E H Q A T A M A D I  
 SEQ. ID. NO. 27 S R Y D Y F A R T V P P D F F Q A K A M A E I L R

FIG. 10a.

SUBSTITUTE SHEET (RULE 26)

58/III

SEQ. ID. NO. 39 YQAQAMVDIVTALGWNYVSTLASEG  
 SEQ. ID. NO. 35 FFNWTYVSTVASSEGDYGETGIEAFE  
 SEQ. ID. NO. 31 IEYFRWNWVGTTAADDYGRPGIEK  
 SEQ. ID. NO. 27 FFNWTYVSTEASSEGDYGETGIEAFE

SEQ. ID. NO. 39 NYGESGVEAFTQISREIGGVCI AQ S  
 SEQ. ID. NO. 35 LEARARNICVATSEKVGGRAMSRAAF  
 SEQ. ID. NO. 31 FREEAEERDIDFSELISQYSDEE  
 SEQ. ID. NO. 27 LEARARNICVATSEKVGGRAMSRAAF

SEQ. ID. NO. 39 QKIPREPRPGEFEKIIKRLLLETPNA  
 SEQ. ID. NO. 35 EGVVRALLQKPSARVAVLFTTRSEDA  
 SEQ. ID. NO. 31 EIQHVVEVIQNSTAKVIVVFSSGPD  
 SEQ. ID. NO. 27 EGVVRALLQKPSARVAVLFTTRSEDA

SEQ. ID. NO. 39 RAVIMFANEDDIRRILEAAKKLNQS  
 SEQ. ID. NO. 35 REL LAASQRLNASFTWVASD GWGAL  
 SEQ. ID. NO. 31 LEPLIKEIVRRNITGKIWLASEAWA  
 SEQ. ID. NO. 27 REL LAASQRLNASFTWVASD GWGAL

SEQ. ID. NO. 39 GHFLWIGSDSWGSKIAPVYQQEEIA  
 SEQ. ID. NO. 35 ESVVAGSEGA AEGAITIELASYPIS  
 SEQ. ID. NO. 31 SSSLIAM PQYFHVVG GTIGFALKAG  
 SEQ. ID. NO. 27 ESVVAGSEGA AEGAITIELASYPIS

SEQ. ID. NO. 39 EGAVTILPKRASIDGFD RYFRSRTL  
 SEQ. ID. NO. 35 DFASYFQSLDPWNN SRNPWFREFWE  
 SEQ. ID. NO. 31 QIPGFREFLKKVHPRKSVHNGFAKE  
 SEQ. ID. NO. 27 DFASYFQSLDPWNN SRNPWFREFWE

SEQ. ID. NO. 39 ANNRRNVWF AEFWEENFGCKLGSHG  
 SEQ. ID. NO. 35 QRFRC SFRQRDCAAHSLRAVPFEQE  
 SEQ. ID. NO. 31 FWEETFNCHLQEGAKGPLPVD TFLR  
 SEQ. ID. NO. 27 QRFRC SFRQRDCAAHSLRAVPFEQE

SEQ. ID. NO. 39 KRNSHIKKCTGLERIARDSSSYEQEG  
 SEQ. ID. NO. 35 SKIMFVVNAVYAMAHALHNMHRALC  
 SEQ. ID. NO. 31 GHEESGDRFSNSSTA FRPLCTGDEN  
 SEQ. ID. NO. 27 SKIMFVVNAVYAMAHALHNMHRALC

FIG. 10b.

59/III

SEQ. ID. NO. 39 K V Q F V I D A V Y S M A Y A L H N M H K D L C P  
 SEQ. ID. NO. 35 P N T T R L C D A M R P V N G R R L Y K D F V L N  
 SEQ. ID. NO. 31 I S S V E T P Y I D Y T H L R I S Y N V Y L A V Y  
 SEQ. ID. NO. 27 P N T T R L C D A M R P V N G R R L Y K D F V L N

SEQ. ID. NO. 39 G Y I G L C P R M S T I D G K E L L G Y I R A V N  
 SEQ. ID. NO. 35 V K F D A P F R P A D T H N E V R F D R F G D G I  
 SEQ. ID. NO. 31 S I A H A L Q D I Y T C L P G R G L F T N G S C A  
 SEQ. ID. NO. 27 V K F D A P F R P A D T H N E V R F D R F G D G I

SEQ. ID. NO. 39 F N G S A G T P V T F N E N G D A P G R Y D I F Q  
 SEQ. ID. NO. 35 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A  
 SEQ. ID. NO. 31 D I K K V E A W Q V L K H L R H L N F T N N M G E  
 SEQ. ID. NO. 27 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A

SEQ. ID. NO. 39 Y Q I T N K S T E Y K V I G H W T N Q L H L K V E  
 SEQ. ID. NO. 35 E G L T L D T S L I P W A S P S A G P L P A S R C  
 SEQ. ID. NO. 31 Q V T F D E C G D L V G N Y S I I N W H L S P E D  
 SEQ. ID. NO. 27 E G L T L D T S L I P W A S P S A G P L A A S R C

SEQ. ID. NO. 39 D M Q W A H R E H T H P A S V C S L P C K P G E R  
 SEQ. ID. NO. 35 S E P C L Q N E V K S V Q P G E V C C W L C I P C  
 SEQ. ID. NO. 31 G S I V F K E V G Y Y N V Y A K K G E R L F I N E  
 SEQ. ID. NO. 27 S E P C L Q N E V K S V Q P G E V C C W L C I P C

SEQ. ID. NO. 39 K K T V K G V P C C W H C E R C E G Y N Y Q V D E  
 SEQ. ID. NO. 35 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L  
 SEQ. ID. NO. 31 E K I L W S G F S R E V P F S N C S R D C L A G T  
 SEQ. ID. NO. 27 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L

SEQ. ID. NO. 39 L S C E L C P L D Q R P N M N R T G C Q L I P I I  
 SEQ. ID. NO. 35 T G C F E L P Q E Y I R W G D A W A V G P V T I A  
 SEQ. ID. NO. 31 R K G I I E G E P T C C F E C V E C P D G E Y S D  
 SEQ. ID. NO. 27 T G C F E L P Q E Y I R W G D A W A V G P V T I A

SEQ. ID. NO. 39 K L E W H S P W A V V P V F V A I L G I I A T T F  
 SEQ. ID. NO. 35 C L G A L A T L F V L G V F V R H N A T P V V K A  
 SEQ. ID. NO. 31 E T D A S A C N K C P D D F W S N E N H T S C F E  
 SEQ. ID. NO. 27 C L G A L A T L F V L G V F V R H N A T P V V K A

FIG. 10c.

60/III

SEQ. ID. NO. 39 V I V T F V R Y N D T P I V R A S G R E L S Y V L  
 SEQ. ID. NO. 35 S G R E L C Y I L L G G V F L C Y C M T F I F I A  
 SEQ. ID. NO. 31 L P Q E Y I R W G D A W A V G P V T I A C L G A L  
 SEQ. ID. NO. 27 S G R E L C Y I L L G G V F L C Y C M T F I F I A

SEQ. ID. NO. 39 L T G I F L C Y S I T F L M I A A P D T I I C S F  
 SEQ. ID. NO. 35 K P S T A V C T L R R L G L G T A F S V C Y S A L  
 SEQ. ID. NO. 31 A T L F V L G V F V R H N A T P V V K A S G R E L  
 SEQ. ID. NO. 27 K P S T A V C T L R R L G L G T A F S V C Y S A L

SEQ. ID. NO. 39 R R V F L G L G M C F S Y A A L L T K T N R I H R  
 SEQ. ID. NO. 35 L T K T N R I A R I F G G A R E G A Q R P R F I S  
 SEQ. ID. NO. 31 C Y I L L G G V F L C Y C M T F I F I A K P S T A  
 SEQ. ID. NO. 27 L T K T N R I A R I F G G A R E G A Q R P R F I S

SEQ. ID. NO. 39 I F E Q G K K S V T A P K F I S P A S Q L V I T F  
 SEQ. ID. NO. 35 P A S Q V A I C L A L I S G Q L L I V V A W L V V  
 SEQ. ID. NO. 31 V C T L R R L G L G T A F S V C Y S A L L T K T N  
 SEQ. ID. NO. 27 P A S Q V A I C L A L I S G Q L L I V V A W L V V

SEQ. ID. NO. 39 S L I S V Q L L G V F V W F V V D P P H I I I D Y  
 SEQ. ID. NO. 35 E A P G T G K E T A P E R R E V V T L R C N H R D  
 SEQ. ID. NO. 31 R I A R I F G G A R E G A Q R P R F I S P A S Q V  
 SEQ. ID. NO. 27 E A P G T G K E T A P E R R E V V T L R C N H R D

SEQ. ID. NO. 39 G E Q R T L D P E K A R G V L K C D I S D L S L I  
 SEQ. ID. NO. 35 A S M L G S L A Y N V L L I A L C T L Y A F K T R  
 SEQ. ID. NO. 31 A I C L A L I S G Q L L I V V A W L V V E A P G T  
 SEQ. ID. NO. 27 A S M L G S L A Y N V L L I A L C T L Y A F N T R

SEQ. ID. NO. 39 C S L G Y S I L L M V T C T V Y A I K T R G V P E  
 SEQ. ID. NO. 35 K C P E N F N E A K F I G F T M Y T T C I I W L A  
 SEQ. ID. NO. 31 G K E T A P E R R E V V T L R C N H R D A S M L G  
 SEQ. ID. NO. 27 K C P E N F N E A K F I G F T M Y T T C I I W L A

SEQ. ID. NO. 39 T F N E A K P I G F T M Y T T C I I W L A F I P I  
 SEQ. ID. NO. 35 F L P I F Y V T S S D Y R V Q T T T M C V S V S L  
 SEQ. ID. NO. 31 S L A Y N V L L I A L C T L Y A F N T R K C P E N  
 SEQ. ID. NO. 27 L L P I F Y V T S S D Y R V Q T T T M C V S V S L

FIG. 10d.

61/III

SEQ. ID. NO. 39 F F G T A Q S A E K M Y I Q T T T L T V S M S L S  
 SEQ. ID. NO. 35 S G S V V L G C L F A P K L H I I L F Q P Q K N T  
 SEQ. ID. NO. 31 F N E A K F I G F T M Y T T C I I W L A L L P I F  
 SEQ. ID. NO. 27 S G S V V L G C L F A P K L H I I L F Q P Q K N

SEQ. ID. NO. 39 A S V S L G M L Y M P K V Y I I I F H P E Q N T I  
 SEQ. ID. NO. 35 I E E V R C S T A A H A F K V A A R A T L R R S N  
 SEQ. ID. NO. 31 Y V T S S D Y R V Q T T T M C V S V S L S G S V V  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 E E V R C S T A A H A F K V A A R A T L R R S N V  
 SEQ. ID. NO. 35 V S R K R S S S L G G S T G S T P S S S I S S K S  
 SEQ. ID. NO. 31 L G C L F A P K L H I I L F Q P Q K N V V S H R A  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 S R K R S S S L G G S T G S T P S S S I S S K S N  
 SEQ. ID. NO. 35 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q  
 SEQ. ID. NO. 31 P T S R F G S A A A R A S S S L G Q G S G S Q F V  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q  
 SEQ. ID. NO. 35 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F  
 SEQ. ID. NO. 31 P T V C N G R E V V D S T T S S L  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F G  
 SEQ. ID. NO. 35 G S G T V T F S L S F D E P Q K N A M A H G N S T  
 SEQ. ID. NO. 31  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 S G T V T F S L S F D E P Q K N A M A H G N S T H  
 SEQ. ID. NO. 35 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C  
 SEQ. ID. NO. 31  
 SEQ. ID. NO. 27

SEQ. ID. NO. 39 Q N S L E A Q K S S D T L T R H Q P L L P L Q C G  
 SEQ. ID. NO. 35 G E T D L D L T V Q E T G L Q G P V G G D Q R P E  
 SEQ. ID. NO. 31  
 SEQ. ID. NO. 27

FIG. 10e.

62/III

SEQ. ID. NO. 39 E T D L D L T V Q E T G L Q G P V G G D Q R P E V  
SEQ. ID. NO. 35 V E D P E E L S P A L V V S S S Q S F V I S G G G  
SEQ. ID. NO. 31  
SEQ. ID. NO. 27

SEQ. ID. NO. 39 E D P E E L S P A L V V S S S Q S F V I S G G G S  
SEQ. ID. NO. 35 S T V T E N V V N S  
SEQ. ID. NO. 31  
SEQ. ID. NO. 27

SEQ. ID. NO. 39 T V T E N V V N S  
SEQ. ID. NO. 35  
SEQ. ID. NO. 31  
SEQ. ID. NO. 27

*FIG. 10f.*

63/III

## ClustalW Formatted Alignments

SEQ. ID. NO. 40 A T G G T A T G C G A G G G A A A G C G A T C A G  
SEQ. ID. NO. 46 A T G G G A T C G C T G C T T G C G C T C C C G G  
SEQ. ID. NO. 36 A T G G G A T C G C T G C T T G C G C T C C C G G  
SEQ. ID. NO. 32 A T G G C A T T T T A T A G C T G C T G C T G G G

SEQ. ID. NO. 40 C C T C T T G C C C T T G T T T C T T C C T C T T  
SEQ. ID. NO. 46 C A C T G C T G C T G C T G T G G G G T G C T G T  
SEQ. ID. NO. 36 C A C T G C T G C T G C T G T G G G G T G C T G T  
SEQ. ID. NO. 32 T C C T C T T G G C A C T C A C C T G G C A C A C

SEQ. ID. NO. 40 G A C C G C C A A G T T C T A C T G G A T C C T C  
SEQ. ID. NO. 46 G G C T G A G G G C C C A G C C A A G A A G G T G  
SEQ. ID. NO. 36 G G C T G A G G G C C C A G C C A A G A A G G T G  
SEQ. ID. NO. 32 C T C T G C C T A C G G G C C A G A C C A G C G A

SEQ. ID. NO. 40 A C A A T G A T G C A A A G A A C T C A C A G C C  
SEQ. ID. NO. 46 C T G A C C C T G G A G G G A G A C T T G G T G C  
SEQ. ID. NO. 36 C T G A C C C T G G A G G G A G A C T T G G T G C  
SEQ. ID. NO. 32 G C C C A A A A G A A A G G G G G A C A T T A T C C

SEQ. ID. NO. 40 A G G A G T A T G C C C A T T C C A T A C G G G T  
SEQ. ID. NO. 46 T G G G T G G G C T G T T C C C A G T G C A C C A  
SEQ. ID. NO. 36 T G G G T G G G C T G T T C C C A G T G C A C C A  
SEQ. ID. NO. 32 T T G G G G G G C T C T T T C C T A T T C A T T T

SEQ. ID. NO. 40 G G A T G G G G A C A T T A T T T T G G G G G G T  
SEQ. ID. NO. 46 G A A G G G C G G C C C A G C A G A G G A C T G T  
SEQ. ID. NO. 36 G A A G G G C G G C C C A G C A G A G G A C T G T  
SEQ. ID. NO. 32 T G G A G T A G C A G C T A A A G A T C A A G A T

SEQ. ID. NO. 40 C T C T T C C C T G T C C A C G C A A A G G G A G  
SEQ. ID. NO. 46 G G T C C T G T C A A T G A G C A C C G T G G C A  
SEQ. ID. NO. 36 G G T C C T G T C A A T G A G C A C C G T G G C A  
SEQ. ID. NO. 32 C T C A A A T C A A G G C C G G A G T C T G T G G

SEQ. ID. NO. 40 A G A G A G G G G T G C C T T G T G G G G A G C T  
SEQ. ID. NO. 46 T C C A G C G C C T G G A G G C C A T G C T T T T  
SEQ. ID. NO. 36 T C C A G C G C C T G G A G G C C A T G C T T T T  
SEQ. ID. NO. 32 A A T G T A T C A G G T A T A A T T T C C G T G G

FIG. 11a.

64/III

SEQ. ID. NO. 40 G A A G A A G G A A A G G G G A T T C A C A G A  
SEQ. ID. NO. 46 T G C A C T G G A C C G C A T C A A C C G T G A C  
SEQ. ID. NO. 36 T G C A C T G G A C C G C A T C A A C C G T G A C  
SEQ. ID. NO. 32 G T T T C G C T G G T T A C A G G C T A T G A T A

SEQ. ID. NO. 40 C T G G A G G C C A T G C T T T A T G C A A T T G  
SEQ. ID. NO. 46 C C G C A C C T G C T G C C T G G C G T G C G C C  
SEQ. ID. NO. 36 C C G C A C C T G C T G C C T G G C G T G C G C C  
SEQ. ID. NO. 32 T T T G C C A T A G A G G A G A T A A A C A G C A

SEQ. ID. NO. 40 A C C A G A T T A A C A A G G A C C C T G A T C T  
SEQ. ID. NO. 46 T G G G T G C A C A C A T C C T C G A C A G T T G  
SEQ. ID. NO. 36 T G G G T G C A C A C A T C C T C G A C A G T T G  
SEQ. ID. NO. 32 G C C C A G C C C T T C T T C C C A A C T T G A C

SEQ. ID. NO. 40 C C T T T C C A A C A T C A C T C T G G G T G T C  
SEQ. ID. NO. 46 C T C C A A G G A C A C A C A T G C G C T G G A G  
SEQ. ID. NO. 36 C T C C A A G G A C A C A C A T G C G C T G G A G  
SEQ. ID. NO. 32 G C T G G G A T A C A G G A T A T T T G A C A C T

SEQ. ID. NO. 40 C G C A T C C T C G A C A C G T G C T C T A G G G  
SEQ. ID. NO. 46 C A G G C A C T G G A C T T T G T G C G T G C C T  
SEQ. ID. NO. 36 C A G G C A C T G G A C T T T G T G C G T G C C T  
SEQ. ID. NO. 32 T G C A A C A C C G T T T C T A A G G C C T T G G

SEQ. ID. NO. 40 A C A C C T A T G C T T T G G A G C A G T C T C T  
SEQ. ID. NO. 46 C A C T C A G C C G T G G T G C T G A T G G C T C  
SEQ. ID. NO. 36 C A C T C A G C C G T G G T G C T G A T G G C T C  
SEQ. ID. NO. 32 A A G C C A C C C T G A G T T T T G T T G C T C A

SEQ. ID. NO. 40 A A C A T T C G T G C A G G C A T T A A T A G A G  
SEQ. ID. NO. 46 A C G C C A C A T C T G C C C C G A C G G C T C T  
SEQ. ID. NO. 36 A C G C C A C A T C T G C C C C G A C G G C T C T  
SEQ. ID. NO. 32 A A A C A A A A T T G A T T C T T T G A A C C T T

SEQ. ID. NO. 40 A A A G A T G C T T C G G A T G T G A A G T G T G  
SEQ. ID. NO. 46 T A T G C G A C C C A T G G T G A T G C T C C C A  
SEQ. ID. NO. 36 T A T G C G A C C C A T G G T G A T G C T C C C A  
SEQ. ID. NO. 32 G A T G A G T T C T G C A A C T G C T C A G A G C

FIG. 11b.



65/III

SEQ. ID. NO. 40 C T A A T G G A G A T C C A C C C A T T T T C A C  
SEQ. ID. NO. 46 C T G C C A T C A C T G G T G T T A T T G G C G G  
SEQ. ID. NO. 36 C T G C C A T C A C T G G T G T T A T T G G C G G  
SEQ. ID. NO. 32 A C A T T C C C T C T A C G A T T G C T G T G G T

SEQ. ID. NO. 40 C A A G C C C G A C A A G A T T T C T G G C G T C  
SEQ. ID. NO. 46 T T C C T A C A G T G A T G T C T C C A T C C A G  
SEQ. ID. NO. 36 T T C C T A C A G T G A T G T C T C C A T C C A G  
SEQ. ID. NO. 32 G G G A G C A A C T G G C T C A G G C G T C T C C

SEQ. ID. NO. 40 A T A G G T G C T G C A G C A A G C T C C G T G T  
SEQ. ID. NO. 46 G T G G C C A A C C T C T T G A G G C T A T T T C  
SEQ. ID. NO. 36 G T G G C C A A C C T C T T G A G G C T A T T T C  
SEQ. ID. NO. 32 A C G G C A G T G G C A A A T C T G C T G G G G C

SEQ. ID. NO. 40 C C A T C A T G G T T G C T A A C A T T T T A A G  
SEQ. ID. NO. 46 A G A T C C C A C A G A T T A G C T A C G C C T C  
SEQ. ID. NO. 36 A G A T C C C A C A G A T T A G C T A C G C C T C  
SEQ. ID. NO. 32 T C T T C T A C A T T C C C C A G G T C A G T T A

SEQ. ID. NO. 40 A C T T T T T A A G A T A C C T C A A A T C A G C  
SEQ. ID. NO. 46 T A C C A G T G C C A A G C T G A G T G A C A A G  
SEQ. ID. NO. 36 T A C C A G T G C C A A G C T G A G T G A C A A G  
SEQ. ID. NO. 32 T G C C T C C T C C A G C A G A C T C C T C A G C

SEQ. ID. NO. 40 T A T G C A T C C A C A G C C C C A G A G C T A A  
SEQ. ID. NO. 46 T C C C G C T A T G A C T A C T T T T G C C C G C A  
SEQ. ID. NO. 36 T C C C G C T A T G A C T A C T T T T G C C C G C A  
SEQ. ID. NO. 32 A A C A A G A A T C A A T T C A A G T C T T T C C

SEQ. ID. NO. 40 G T G A T A A C A C C A G G T A T G A C T T T T T  
SEQ. ID. NO. 46 C A G T G C C T C C T G A C T T C T T C C A A G C  
SEQ. ID. NO. 36 C A G T G C C T C C T G A C T T C T T C C A A G C  
SEQ. ID. NO. 32 T C C G A A C C A T C C C C A A T G A T G A G C A

SEQ. ID. NO. 40 C T C T C G A G T G G T T C C G C C T G A C T C C  
SEQ. ID. NO. 46 C A A G G C C A T G G C T G A G A T T C T C C G C  
SEQ. ID. NO. 36 C A A G G C C A T G G C T G A G A T T C T C C G C  
SEQ. ID. NO. 32 C C A G G C C A C T G C C A T G G C A G A C A T C

FIG. 1/c.

66/III

SEQ. ID. NO. 40 T A C C A A G C C C A A G C C A T G G T G G A C A  
SEQ. ID. NO. 46 T T C T T C A A C T G G A C C T A T G T G T C C A  
SEQ. ID. NO. 36 T T C T T C A A C T G G A C C T A T G T G T C C A  
SEQ. ID. NO. 32 A T C G A G T A T T T C C G C T G G A A C T G G G

SEQ. ID. NO. 40 T C G T G A C A G C A C T G G G A T G G A A T T A  
SEQ. ID. NO. 46 C T G T G G C G T C T G A G G G C G A C T A T G G  
SEQ. ID. NO. 36 C T G T G G C G T C T G A G G G C G A C T A T G G  
SEQ. ID. NO. 32 T G G G C A C A A T T G C A G C T G A T G A C G A

SEQ. ID. NO. 40 T G T T T C G A C A C T G G C T T C T G A G G G G  
SEQ. ID. NO. 46 C G A G A C A G G C A T T G A G G C C T T T G A G  
SEQ. ID. NO. 36 C G A G A C A G G C A T T G A G G C C T T T G A G  
SEQ. ID. NO. 32 C T A T G G G C G G C C G G G G A T T G A G A A A

SEQ. ID. NO. 40 A A C T A T G G T G A G A G C G G T G T G G A G G  
SEQ. ID. NO. 46 C T A G A G G C T C G T G C C C G C A A C A T C T  
SEQ. ID. NO. 36 C T A G A G G C T C G T G C C C G C A A C A T C T  
SEQ. ID. NO. 32 T T C C G A G A G G A A G C T G A G G A A A G G G

SEQ. ID. NO. 40 C C T T C A C C C A G A T C T C G A G G G A G A T  
SEQ. ID. NO. 46 G T G T G G C C A C C T C G G A G A A A G T G G G  
SEQ. ID. NO. 36 G T G T G G C C A C C T C G G A G A A A G T G G G  
SEQ. ID. NO. 32 A T A T C T G C A T C G A C T T C A G T G A A C T

SEQ. ID. NO. 40 T G G T G G T G T T T G C A T T G C T C A G T C A  
SEQ. ID. NO. 46 C C G T G C C A T G A G C C G C G C G G C C T T T  
SEQ. ID. NO. 36 C C G T G C C A T G A G C C G C G C G G C C T T T  
SEQ. ID. NO. 32 C A T C T C C A G T A C T C T G A T G A G G A A

SEQ. ID. NO. 40 C A G A A A A T C C C A C G T G A A C C A A G A C  
SEQ. ID. NO. 46 G A G G G T G T G G T G C G A G C C C T G C T G C  
SEQ. ID. NO. 36 G A G G G T G T G G T G C G A G C C C T G C T G C  
SEQ. ID. NO. 32 G A G A T C C A G C A T G T G G T A G A G G T G A

SEQ. ID. NO. 40 C T G G A G A A T T T G A A A A A A T T A T C A A  
SEQ. ID. NO. 46 A G A A G C C C A G T G C C C G C G T G G C T G T  
SEQ. ID. NO. 36 A G A A G C C C A G T G C C C G C G T G G C T G T  
SEQ. ID. NO. 32 T T C A A A A T T C C A C G G C C A A A G T C A T

*FIG. 1Id.*

67/III

SEQ. ID. NO. 40 A C G C C T G C T A G A A A C A C C T A A T G C T  
SEQ. ID. NO. 46 C C T G T T C A C C C G T T C T G A G G A T G C C  
SEQ. ID. NO. 36 C C T G T T C A C C C G T T C T G A G G A T G C C  
SEQ. ID. NO. 32 C G T G G T T T T C T C C A G T G G C C C A G A T

SEQ. ID. NO. 40 C G A G C A G T G A T T A T G T T T G C C A A T G  
SEQ. ID. NO. 46 C G G G A G C T G C T T G C T G C C A G C C A G C  
SEQ. ID. NO. 36 C G G G A G C T G C T T G C T G C C A G C C A G C  
SEQ. ID. NO. 32 C T T G A G C C C C T C A T C A A G G A G A T T G

SEQ. ID. NO. 40 A G G A T G A C A T C A G G A G G A T A T T G G A  
SEQ. ID. NO. 46 G C C T C A A T G C C A G C T T C A C C T G G G T  
SEQ. ID. NO. 36 G C C T C A A T G C C A G C T T C A C C T G G G T  
SEQ. ID. NO. 32 T C C G G C G C A A T A T C A C G G G C A A G A T

SEQ. ID. NO. 40 A G C A G C A A A A A A A C T A A A C C A A A G T  
SEQ. ID. NO. 46 G G C C A G T G A T G G T T G G G G G G C C C T G  
SEQ. ID. NO. 36 G G C C A G T G A T G G T T G G G G G G C C C T G  
SEQ. ID. NO. 32 C T G G C T G G C C A G C G A G G C C T G G G C C

SEQ. ID. NO. 40 G G G C A T T T T C T C T G G A T T G G C T C A G  
SEQ. ID. NO. 46 G A G A G T G T G G T G G C A G G C A G T G A G G  
SEQ. ID. NO. 36 G A G A G T G T G G T G G C A G G C A G T G A G G  
SEQ. ID. NO. 32 A G C T C C T C C C T G A T C G C C A T G C C T C

SEQ. ID. NO. 40 A T A G T T G G G G A T C C A A A A T A G C A C C  
SEQ. ID. NO. 46 G G G C T G C T G A G G G T G C T A T C A C C A T  
SEQ. ID. NO. 36 G G G C T G C T G A G G G T G C T A T C A C C A T  
SEQ. ID. NO. 32 A G T A C T T C C A C G T G G T T G G C G G C A C

SEQ. ID. NO. 40 T G T C T A T C A G C A A G A G G A G A T T G C A  
SEQ. ID. NO. 46 C G A G C T G G C C T C C T A C C C C A T C A G T  
SEQ. ID. NO. 36 C G A G C T G G C C T C C T A C C C C A T C A G T  
SEQ. ID. NO. 32 C A T T G G A T T C G C T C T G A A G G C T G G G

SEQ. ID. NO. 40 G A A G G G G C T G T G A C A A T T T T G C C C A  
SEQ. ID. NO. 46 G A C T T T G C C T C C T A C T T C C A G A G C C  
SEQ. ID. NO. 36 G A C T T T G C C T C C T A C T T C C A G A G C C  
SEQ. ID. NO. 32 C A G A T C C C A G G C T T C C G G G A A T T C C

*FIG. 11e.*

68/III

SEQ. ID. NO. 40 A A C G A G C A T C A A T T G A T G G A T T T G A  
SEQ. ID. NO. 46 T G G A C C C T T G G A A C A A C A G C C G G A A  
SEQ. ID. NO. 36 T G G A C C C T T G G A A C A A C A G C C G G A A  
SEQ. ID. NO. 32 T G A A G A A G G T C C A T C C C A G G A A G T C

SEQ. ID. NO. 40 T C G A T A C T T T A G A A G C C G A A C T C T T  
SEQ. ID. NO. 46 C C C C T G G T T C C G T G A A T T C T G G G A G  
SEQ. ID. NO. 36 C C C C T G G T T C C G T G A A T T C T G G G A G  
SEQ. ID. NO. 32 T G T C C A C A A T G G T T T T G C C A A G G A G

SEQ. ID. NO. 40 G C C A A T A A T C G A A G A A A T G T G T G G T  
SEQ. ID. NO. 46 C A G A G G T T C C G C T G C A G C T T C C G G C  
SEQ. ID. NO. 36 C A G A G G T T C C G C T G C A G C T T C C G G C  
SEQ. ID. NO. 32 T T T T G G G A A G A A A C A T T T A A C T G C C

SEQ. ID. NO. 40 T T G C A G A A T T C T G G G A G G A G A A T T T  
SEQ. ID. NO. 46 A G C G A G A C T G C G C A G C C C A C T C T C T  
SEQ. ID. NO. 36 A G C G A G A C T G C G C A G C C C A C T C T C T  
SEQ. ID. NO. 32 A C C T C C A A G A A G G T G C A A A A G G A C C

SEQ. ID. NO. 40 T G G C T G C A A G T T A G G A T C A C A T G G G  
SEQ. ID. NO. 46 C C G G G C T G T G C C C T T T G A G C A G G A G  
SEQ. ID. NO. 36 C C G G G C T G T G C C C T T T G A G C A G G A G  
SEQ. ID. NO. 32 T T T A C C T G T G G A C A C C T T T C T G A G A

SEQ. ID. NO. 40 A A A A G G A A C A G T C A T A T A A A G A A A T  
SEQ. ID. NO. 46 T C C A A G A T C A T G T T T G T G G T C A A T G  
SEQ. ID. NO. 36 T C C A A G A T C A T G T T T G T G G T C A A T G  
SEQ. ID. NO. 32 G G T C A C G A A G A A A G T G G C G A C A G G T

SEQ. ID. NO. 40 G C A C A G G G C T G G A G C G A A T T G C T C G  
SEQ. ID. NO. 46 C A G T G T A C G C C A T G G C C C A T G C G C T  
SEQ. ID. NO. 36 C A G T G T A C G C C A T G G C C C A T G C G C T  
SEQ. ID. NO. 32 T T A G C A A C A G C T C G A C A G C C T T C C G

SEQ. ID. NO. 40 G G A T T C A T C T T A T G A A C A G G A A G G A  
SEQ. ID. NO. 46 C C A C A A C A T G C A C C G T G C C C T C T G C  
SEQ. ID. NO. 36 C C A C A A C A T G C A C C G T G C C C T C T G C  
SEQ. ID. NO. 32 A C C C C T C T G T A C A G G G G A T G A G A A C

*FIG. 11f.*

SUBSTITUTE SHEET (RULE 26)

69/III

SEQ. ID. NO. 40 A A G G T C C A A T T T G T A A T T G A T G C T G  
SEQ. ID. NO. 46 C C C A A C A C C A C C C G G C T C T G T G A C G  
SEQ. ID. NO. 36 C C C A A C A C C A C C C G G C T C T G T G A C G  
SEQ. ID. NO. 32 A T C A G C A G T G T C G A G A C C C C T T A C A

SEQ. ID. NO. 40 T A T A T T C C A T G G C T T A C G C C C T G C A  
SEQ. ID. NO. 46 C G A T G C G G C C A G T T A A C G G G C G C C G  
SEQ. ID. NO. 36 C G A T G C G G C C A G T T A A C G G G C G C C G  
SEQ. ID. NO. 32 T A G A T T A C A C G C A T T T A C G G A T A T C

SEQ. ID. NO. 40 C A A T A T G C A C A A A G A T C T C T G C C C T  
SEQ. ID. NO. 46 C C T C T A C A A G G A C T T T G T G C T C A A C  
SEQ. ID. NO. 36 C C T C T A C A A G G A C T T T G T G C T C A A C  
SEQ. ID. NO. 32 C T A C A A T G T G T A C T T A G C A G T C T A C

SEQ. ID. NO. 40 G G A T A C A T T G G C C T T T G T C C A C G A A  
SEQ. ID. NO. 46 G T C A A G T T T G A T G C C C C C T T T C G C C  
SEQ. ID. NO. 36 G T C A A G T T T G A T G C C C C C T T T C G C C  
SEQ. ID. NO. 32 T C C A T T G C C C A C G C C T T G C A A G A T A

SEQ. ID. NO. 40 T G A G T A C C A T T G A T G G G A A A G A G C T  
SEQ. ID. NO. 46 C A G C T G A C A C C C A C A A T G A G G T C C G  
SEQ. ID. NO. 36 C A G C T G A C A C C C A C A A T G A G G T C C G  
SEQ. ID. NO. 32 T A T A T A C C T G C T T A C C T G G G A G A G G

SEQ. ID. NO. 40 A C T T G G T T A T A T T C G G G C T G T A A A T  
SEQ. ID. NO. 46 C T T T G A C C G C T T T G G T G A T G G T A T T  
SEQ. ID. NO. 36 C T T T G A C C G C T T T G G T G A T G G T A T T  
SEQ. ID. NO. 32 G C T C T T C A C C A A T G G C T C C T G T G C A

SEQ. ID. NO. 40 T T T A A T G G C A G T G C T G G C A C T C C T G  
SEQ. ID. NO. 46 G G C C G C T A C A A C A T C T T C A C C T A T C  
SEQ. ID. NO. 36 G G C C G C T A C A A C A T C T T C A C C T A T C  
SEQ. ID. NO. 32 G A C A T C A A G A A A G T T G A G G C G T G G C

SEQ. ID. NO. 40 T C A C T T T T A A T G A A A C G G A G A T G C  
SEQ. ID. NO. 46 T G C G T G C A G G C A G T G G G C G C T A T C G  
SEQ. ID. NO. 36 T G C G T G C A G G C A G T G G G C G C T A T C G  
SEQ. ID. NO. 32 A G G T C C T G A A G C A C C T A C G G C A T C T

*FIG. 11g.*

SUBSTITUTE SHEET (RULE 26)

70/III

SEQ. ID. NO. 40 T C C T G G A C G T T A T G A T A T C T T C C A G  
SEQ. ID. NO. 46 C T A C C A G A A G G T G G G C T A C T G G G C A  
SEQ. ID. NO. 36 C T A C C A G A A G G T G G G C T A C T G G G C A  
SEQ. ID. NO. 32 A A A C T T T A C A A A C A A T A T G G G G G A G

SEQ. ID. NO. 40 T A T C A A A T A A C C A A C A A A A G C A C A G  
SEQ. ID. NO. 46 G A A G G C T T G A C T C T G G A C A C C A G C C  
SEQ. ID. NO. 36 G A A G G C T T G A C T C T G G A C A C C A G C C  
SEQ. ID. NO. 32 C A G G T G A C C T T T G A T G A G T G T G G T G

SEQ. ID. NO. 40 A G T A C A A A G T C A T C G G C C A C T G G A C  
SEQ. ID. NO. 46 T C A T C C C A T G G G C C T C A C C C T C A G C  
SEQ. ID. NO. 36 T C A T C C C A T G G G C C T C A C C C T C A G C  
SEQ. ID. NO. 32 A C C T G G T G G G G A A C T A T T C C A T C A T

SEQ. ID. NO. 40 C A A T C A G C T T C A T C T A A A A G T G G A A  
SEQ. ID. NO. 46 C G G C C C C C T G C C C G C C T C T C G C T G C  
SEQ. ID. NO. 36 C G G C C C C C T G C C C G C C T C T C G C T G C  
SEQ. ID. NO. 32 C A A C T G G C A C C T C T C C C C A G A G G A T

SEQ. ID. NO. 40 G A C A T G C A G T G G G C T C A T A G A G A A C  
SEQ. ID. NO. 46 A G T G A G C C C T G C C T C C A G A A T G A G G  
SEQ. ID. NO. 36 A G T G A G C C C T G C C T C C A G A A T G A G G  
SEQ. ID. NO. 32 G G C T C C A T C G T G T T T A A G G A A G T C G

SEQ. ID. NO. 40 A T A C T C A C C C G G C G T C T G T C T G C A G  
SEQ. ID. NO. 46 T G A A G A G T G T G C A G C C G G G C G A A G T  
SEQ. ID. NO. 36 T G A A G A G T G T G C A G C C G G G C G A A G T  
SEQ. ID. NO. 32 G G T A T T A C A A C G T C T A T G C C A A G A A

SEQ. ID. NO. 40 C C T G C C G T G T A A G C C A G G G G A G A G G  
SEQ. ID. NO. 46 C T G C T G C T G G C T C T G C A T T C C G T G C  
SEQ. ID. NO. 36 C T G C T G C T G G C T C T G C A T T C C G T G C  
SEQ. ID. NO. 32 G G G A G A A A G A C T C T T C A T C A A C G A G

SEQ. ID. NO. 40 A A G A A A A C G G T G A A A G G G G T C C C T T  
SEQ. ID. NO. 46 C A G C C C T A T G A G T A C C G A T T G G A C G  
SEQ. ID. NO. 36 C A G C C C T A T G A G T A C C G A T T G G A C G  
SEQ. ID. NO. 32 G A G A A A A T C C T G T G G A G T G G G T T C T

FIG. 11h.

SUBSTITUTE SHEET (RULE 26)

71/III

SEQ. ID. NO. 40 G C T G C T G G C A C T G T G A A C G C T G T G A  
SEQ. ID. NO. 46 A A T T C A C T T G C G C T G A T T G T G G C C T  
SEQ. ID. NO. 36 A A T T C A C T T G C G C T G A T T G T G G C C T  
SEQ. ID. NO. 32 C C A G G G A G G T G C C C T T C T C C A A C T G

SEQ. ID. NO. 40 A G G T T A C A A C T A C C A G G T G G A T G A G  
SEQ. ID. NO. 46 G G G C T A C T G G C C C A A T G C C A G C C T G  
SEQ. ID. NO. 36 G G G C T A C T G G C C C A A T G C C A G C C T G  
SEQ. ID. NO. 32 C A G C C G A G A C T G C C T G G C A G G G A C C

SEQ. ID. NO. 40 C T G T C C T G T G A A C T T T G C C C T C T G G  
SEQ. ID. NO. 46 A C T G G C T G C T T C G A A C T G C C C C A G G  
SEQ. ID. NO. 36 A C T G G C T G C T T C G A A C T G C C C C A G G  
SEQ. ID. NO. 32 A G G A A A G G G A T C A T T G A G G G G G A G C

SEQ. ID. NO. 40 A T C A G A G A C C C A A C A T G A A C C G C A C  
SEQ. ID. NO. 46 A G T A C A T C C G C T G G G G C G A T G C C T G  
SEQ. ID. NO. 36 A G T A C A T C C G C T G G G G C G A T G C C T G  
SEQ. ID. NO. 32 C C A C C T G C T G C T T T G A G T G T G T G G A

SEQ. ID. NO. 40 A G G C T G C C A G C T T A T C C C C A T C A T C  
SEQ. ID. NO. 46 G G C T G T G G G A C C T G T C A C C A T C G C C  
SEQ. ID. NO. 36 G G C T G T G G G A C C T G T C A C C A T C G C C  
SEQ. ID. NO. 32 G T G T C C T G A T G G G G A G T A T A G T G A T

SEQ. ID. NO. 40 A A A T T G G A G T G G C A T T C T C C C T G G G  
SEQ. ID. NO. 46 T G C C T C G G T G C C C T G G C C A C C C T C T  
SEQ. ID. NO. 36 T G C C T C G G T G C C C T G G C C A C C C T C T  
SEQ. ID. NO. 32 G A G A C A G A T G C C A G T G C C T G T A A C A

SEQ. ID. NO. 40 C T G T G G T G C C T G T G T T T G T T G C A A T  
SEQ. ID. NO. 46 T T G T G C T G G G T G T C T T T G T G C G G C A  
SEQ. ID. NO. 36 T T G T G C T G G G T G T C T T T G T G C G G C A  
SEQ. ID. NO. 32 A G T G C C C A G A T G A C T T C T G G T C C A A

SEQ. ID. NO. 40 A T T G G G A A T C A T C G C C A C C A C C T T T  
SEQ. ID. NO. 46 C A A T G C C A C A C C A G T G G T C A A G G C C  
SEQ. ID. NO. 36 C A A T G C C A C A C C A G T G G T C A A G G C C  
SEQ. ID. NO. 32 T G A G A A C C A C A C C T C C T G C T T C G A A

FIG. 11i

SUBSTITUTE SHEET (RULE 26)

72/III

SEQ. ID. NO. 40 GTGATCGTGACCTTTGTCCGCTATA  
SEQ. ID. NO. 46 TCAGGTCGGGAGCTCTGCTACATCC  
SEQ. ID. NO. 36 TCAGGTCGGGAGCTCTGCTACATCC  
SEQ. ID. NO. 32 CTGCCCCAGGAGTACATCCGCTGGG

SEQ. ID. NO. 40 ATGACACACCTATCTGTGAGGGCTTTC  
SEQ. ID. NO. 46 TGCTGGGTGGTGTCTTCTCTGCTA  
SEQ. ID. NO. 36 TGCTGGGTGGTGTCTTCTCTGCTA  
SEQ. ID. NO. 32 GCGATGCCCTGGGCTGTGGGACCTGT

SEQ. ID. NO. 40 AGGACGCGAACTTAGTTACGTGCTC  
SEQ. ID. NO. 46 CTGCATGACCTTTCATCTTTCATTGCC  
SEQ. ID. NO. 36 CTGCATGACCTTTCATCTTTCATTGCC  
SEQ. ID. NO. 32 CACCATCGCCTGCTCTGGGTGCCCTG

SEQ. ID. NO. 40 CTAACGGGGATTTTTCTCTGTTATT  
SEQ. ID. NO. 46 AAGCCATCCACGGGCAGTGTGTACCT  
SEQ. ID. NO. 36 AAGCCATCCACGGGCAGTGTGTACCT  
SEQ. ID. NO. 32 GCCACCCTGTTTGTGCTGGGTGTCT

SEQ. ID. NO. 40 CAATCACGTTTTTTAATGATTGCAAGC  
SEQ. ID. NO. 46 TACGGCGTCTTTGGTTTGGGGCACTGC  
SEQ. ID. NO. 36 TACGGCGTCTTTGGTTTGGGGCACTGC  
SEQ. ID. NO. 32 TTGTGCGGCGACAAATGCCACACCAGT

SEQ. ID. NO. 40 ACCAGATACAATCATATGCTCCTTTC  
SEQ. ID. NO. 46 CTTCTCTGTCTGTCTACTCAGCCCTG  
SEQ. ID. NO. 36 CTTCTCTGTCTGTCTACTCAGCCCTG  
SEQ. ID. NO. 32 GGTC AAGGCCCTCAGGTCGGGAGCTC

SEQ. ID. NO. 40 CGACGGGGTCTTCTCTAGGACTTGGCA  
SEQ. ID. NO. 46 CTCACCAAGACCAACCAGCATTTGCAC  
SEQ. ID. NO. 36 CTCACCAAGACCAACCAGCATTTGCAC  
SEQ. ID. NO. 32 TGCTACATCCTGTGCTGGGTGGTGTCT

SEQ. ID. NO. 40 TGTGTTTTCAGCTATGCAAGCCCTTCT  
SEQ. ID. NO. 46 GCATCTTTCGGTGGGGGCCCGGGAGGG  
SEQ. ID. NO. 36 GCATCTTTCGGTGGGGGCCCGGGAGGG  
SEQ. ID. NO. 32 TCCTCTGTCTACTGCATGACCTTCA

FIG. 11j.

SUBSTITUTE SHEET (RULE 26)



73/III

SEQ. ID. NO. 40 G A C C A A A A C A A A C C G T A T C C A C C G A  
SEQ. ID. NO. 46 T G C C C A G C G G C C A C G C T T C A T C A G T  
SEQ. ID. NO. 36 T G C C C A G C G G C C A C G C T T C A T C A G T  
SEQ. ID. NO. 32 C T T C A T T G C C A A G C C A T C C A C G G C A

SEQ. ID. NO. 40 A T A T T T G A G C A G G G G A A G A A A T C T G  
SEQ. ID. NO. 46 C C T G C C T C A C A G G T G G C C A T C T G C C  
SEQ. ID. NO. 36 C C T G C C T C A C A G G T G G C C A T C T G C C  
SEQ. ID. NO. 32 G T G T G T A C C T T A C G G C G T C T T G G T T

SEQ. ID. NO. 40 T C A C A G C G C C C A A G T T C A T T A G T C C  
SEQ. ID. NO. 46 T G G C A C T T A T C T C G G G C C A G C T G C T  
SEQ. ID. NO. 36 T G G C A C T T A T C T C G G G C C A G C T G C T  
SEQ. ID. NO. 32 T G G G C A C T G C C T T C T C T G T C T G C T A

SEQ. ID. NO. 40 A G C A T C T C A G C T G G T G A T C A C C T T C  
SEQ. ID. NO. 46 C A T C G T G G T C G C C T G G C T G G T G G T G  
SEQ. ID. NO. 36 C A T C G T G G T C G C C T G G C T G G T G G T G  
SEQ. ID. NO. 32 C T C A G C C C T G C T C A C C A A G A C C A A C

SEQ. ID. NO. 40 A G C C T C A T C T C C G T C C A G C T C C T T G  
SEQ. ID. NO. 46 G A G G C A C C G G G C A C A G G C A A G G A G A  
SEQ. ID. NO. 36 G A G G C A C C G G G C A C A G G C A A G G A G A  
SEQ. ID. NO. 32 C G C A T T G C A C G C A T C T T C G G T G G G G

SEQ. ID. NO. 40 G A G T G T T T G T C T G G T T T G T T G T G G A  
SEQ. ID. NO. 46 C A G C C C C C G A A C G G C G G G A G G T G G T  
SEQ. ID. NO. 36 C A G C C C C C G A A C G G C G G G A G G T G G T  
SEQ. ID. NO. 32 C C C G G G A G G G T G C C C A G C G G C C A C G

SEQ. ID. NO. 40 T C C C C C C A C A T C A T C A T T G A C T A T  
SEQ. ID. NO. 46 G A C A C T G C G C T G C A A C C A C C G C G A T  
SEQ. ID. NO. 36 G A C A C T G C G C T G C A A C C A C C G C G A T  
SEQ. ID. NO. 32 C T T C A T C A G T C C T G C C T C A C A G G T G

SEQ. ID. NO. 40 G G A G A G C A G C G G A C A C T A G A T C C A G  
SEQ. ID. NO. 46 G C A A G T A T G T T G G G C T C G C T G G C C T  
SEQ. ID. NO. 36 G C A A G T A T G T T G G G C T C G C T G G C C T  
SEQ. ID. NO. 32 G C C A T C T G C C T G G C A C T T A T C T C G G

FIG. 11k.

74/III

SEQ. ID. NO. 40 A G A A G G C C A G G G G A G T G C T C A A G T G  
SEQ. ID. NO. 46 A C A A T G T G C T C C T C A T C G C G C T C T G  
SEQ. ID. NO. 36 A C A A T G T G C T C C T C A T C G C G C T C T G  
SEQ. ID. NO. 32 G C C A G C T G C T C A T C G T G G T C G C C T G

SEQ. ID. NO. 40 T G A C A T T T C T G A T C T C T C A C T C A T T  
SEQ. ID. NO. 46 C A C G C T T T A T G C C T T C A A G A C T C G C  
SEQ. ID. NO. 36 C A C G C T T T A T G C C T T C A A G A C T C G C  
SEQ. ID. NO. 32 G C T G G T G G T G G A G G C A C C G G G C A C A

SEQ. ID. NO. 40 T G T T C A C T T G G A T A C A G T A T C C T C T  
SEQ. ID. NO. 46 A A G T G C C C C G A A A A C T T C A A C G A G G  
SEQ. ID. NO. 36 A A G T G C C C C G A A A A C T T C A A C G A G G  
SEQ. ID. NO. 32 G G C A A G G A G A C A G C C C C C G A A C G G C

SEQ. ID. NO. 40 T G A T G G T C A C T T G T A C T G T T T A T G C  
SEQ. ID. NO. 46 C C A A G T T C A T T G G C T T C A C C A T G T A  
SEQ. ID. NO. 36 C C A A G T T C A T T G G C T T C A C C A T G T A  
SEQ. ID. NO. 32 G G G A G G T G G T G A C A C T G C G C T G C A A

SEQ. ID. NO. 40 C A T T A A A A C G A G A G G T G T C C C A G A G  
SEQ. ID. NO. 46 C A C C A C C T G C A T C A T C T G G C T G G C A  
SEQ. ID. NO. 36 C A C C A C C T G C A T C A T C T G G C T G G C A  
SEQ. ID. NO. 32 C C A C C G C G A T G C A A G T A T G T T G G G C

SEQ. ID. NO. 40 A C T T T C A A T G A A G C C A A A C C T A T T G  
SEQ. ID. NO. 46 T T C C T G C C C C A T C T T C T A T G T C A C C T  
SEQ. ID. NO. 36 T T C C T G C C C C A T C T T C T A T G T C A C C T  
SEQ. ID. NO. 32 T C G C T G G C C T A C A A T G T G C T C C T C A

SEQ. ID. NO. 40 G A T T T A C C A T G T A T A C C A C C T G C A T  
SEQ. ID. NO. 46 C C A G T G A C T A C C G G G T A C A G A C C A C  
SEQ. ID. NO. 36 C C A G T G A C T A C C G G G T A C A G A C C A C  
SEQ. ID. NO. 32 T C G C G C T C T G C A C G C T T T A T G C C T T

SEQ. ID. NO. 40 C A T T T G G T T A G C T T T C A T C C C C A T C  
SEQ. ID. NO. 46 C A C C A T G T G C G T G T C A G T C A G C C T C  
SEQ. ID. NO. 36 C A C C A T G T G C G T G T C A G T C A G C C T C  
SEQ. ID. NO. 32 C A A T A C T C G C A A G T G C C C C G A A A A C

*FIG. 1/L.*

SUBSTITUTE SHEET (RULE 26)

75/III

SEQ. ID. NO. 40 T T T T T T G G T A C A G C C C A G T C A G C A G  
SEQ. ID. NO. 46 A G C G G C T C C G T G G T G C T T G G C T G C C  
SEQ. ID. NO. 36 A G C G G C T C C G T G G T G C T T G G C T G C C  
SEQ. ID. NO. 32 T T C A A C G A G G C C A A G T T C A T T G G C T

SEQ. ID. NO. 40 A A A A G A T G T A C A T C C A G A C A A C A A C  
SEQ. ID. NO. 46 T C T T T G C G C C C A A G C T G C A C A T C A T  
SEQ. ID. NO. 36 T C T T T G C G C C C A A G C T G C A C A T C A T  
SEQ. ID. NO. 32 T C A C C A T G T A C A C C A C C T G C A T C A T

SEQ. ID. NO. 40 A C T T A C T G T C T C C A T G A G T T T A A G T  
SEQ. ID. NO. 46 C C T C T T C C A G C C G C A G A A G A A C A C C  
SEQ. ID. NO. 36 C C T C T T C C A G C C G C A G A A G A A C A C C  
SEQ. ID. NO. 32 C T G G C T G G C A T T G T T G C C C A T C T T C

SEQ. ID. NO. 40 G C T T C A G T A T C T C T G G G C A T G C T C T  
SEQ. ID. NO. 46 A T C G A G G A G G T G C G T T G C A G C A C C G  
SEQ. ID. NO. 36 A T C G A G G A G G T G C G T T G C A G C A C C G  
SEQ. ID. NO. 32 T A T G T C A C C T C C A G T G A C T A C C G G G

SEQ. ID. NO. 40 A T A T G C C C A A G G T T T A T A T T A T A A T  
SEQ. ID. NO. 46 C A G C T C A C G C T T T C A A G G T G G C T G C  
SEQ. ID. NO. 36 C A G C T C A C G C T T T C A A G G T G G C T G C  
SEQ. ID. NO. 32 T A C A G A C C A C C A C C A T G T G C G T G T C

SEQ. ID. NO. 40 T T T T C A T C C A G A A C A G A A T A C C A T C  
SEQ. ID. NO. 46 C C G G G C C A C G C T G C G C C G C A G C A A C  
SEQ. ID. NO. 36 C C G G G C C A C G C T G C G C C G C A G C A A C  
SEQ. ID. NO. 32 A G T C A G C C T C A G C G G C T C C G T G G T G

SEQ. ID. NO. 40 G A G G A G G T G C G T T G C A G C A C C G C A G  
SEQ. ID. NO. 46 G T C T C C C G C A A G C G G T C C A G C A G C C  
SEQ. ID. NO. 36 G T C T C C C G C A A G C G G T C C A G C A G C C  
SEQ. ID. NO. 32 C T T G G C T G C C T C T T T G C G C C C A A G C

SEQ. ID. NO. 40 C T C A C G C T T T C A A G G T G G C T G C C C G  
SEQ. ID. NO. 46 T T G G A G G C T C C A C G G G A T C C A C C C C  
SEQ. ID. NO. 36 T T G G A G G C T C C A C G G G A T C C A C C C C  
SEQ. ID. NO. 32 T G C A C A T C A T C C T C T T C C A G C C G C A

*FIG. 1 Im.*

SUBSTITUTE SHEET (RULE 26)

76/III

SEQ. ID. NO. 40 G G C C A C G C T G C G C C G C A G C A A C G T C  
SEQ. ID. NO. 46 C T C C T C C T C C A T C A G C A G C A A G A G C  
SEQ. ID. NO. 36 C T C C T C C T C C A T C A G C A G C A A G A G C  
SEQ. ID. NO. 32 G A A G A A C G T G G T T A G C C A C C G G G C A

SEQ. ID. NO. 40 T C C C G C A A G C G G T C C A G C A G C C T T G  
SEQ. ID. NO. 46 A A C A G C G A A G A C C C A T T C C C A C A G C  
SEQ. ID. NO. 36 A A C A G C G A A G A C C C A T T C C C A C A G C  
SEQ. ID. NO. 32 C C C A C C A G C C G C T T T G G C A G T G C T G

SEQ. ID. NO. 40 G A G G C T C C A C G G G A T C C A C C C C C T C  
SEQ. ID. NO. 46 C C G A G A G G C A G A A A G C A G C A G C A G C C  
SEQ. ID. NO. 36 C C G A G A G G C A G A A A G C A G C A G C A G C C  
SEQ. ID. NO. 32 C T G C C A G G G C C A G C T C C A G C C T T G G

SEQ. ID. NO. 40 C T C C T C C A T C A G C A G C A A G A G C A A C  
SEQ. ID. NO. 46 G C T G G C C C T A A C C C A G C A A G A G C A G  
SEQ. ID. NO. 36 G C T G G C C C T A A C C C A G C A A G A G C A G  
SEQ. ID. NO. 32 C C A A G G G T C T G G C T C C C A G T T T G T C

SEQ. ID. NO. 40 A G C G A A G A C C C A T T C C C A C A G C C C G  
SEQ. ID. NO. 46 C A G C A G C A G C C C C T G A C C C T C C C A C  
SEQ. ID. NO. 36 C A G C A G C A G C C C C T G A C C C T C C C A C  
SEQ. ID. NO. 32 C C C A C T G T T T G C A A T G G C C G T G A G G

SEQ. ID. NO. 40 A G A G G C A G A A A G C A G C A G C A G C C G C T  
SEQ. ID. NO. 46 A G C A G C A A C G A T C T C A G C A G C A G C C  
SEQ. ID. NO. 36 A G C A G C A A C G A T C T C A G C A G C A G C C  
SEQ. ID. NO. 32 T G G T G G A C T C G A C A A C G T C A T C G C T

SEQ. ID. NO. 40 G G C C C T A A C C C A G C A A G A G C A G C A G  
SEQ. ID. NO. 46 C A G A T G C A A G C A G A A G G T C A T C T T T  
SEQ. ID. NO. 36 C A G A T G C A A G C A G A A G G T C A T C T T T  
SEQ. ID. NO. 32 T A T G A C T C T G G A G T C C A T C A T G G C G

SEQ. ID. NO. 40 C A G C A G C C C C T G A C C C T C C C A C A G C  
SEQ. ID. NO. 46 G G C A G C G G C A C G G T C A C C T T C T C A C  
SEQ. ID. NO. 36 G G C A G C G G C A C G G T C A C C T T C T C A C  
SEQ. ID. NO. 32 T G C T G C C T G A G C G A G G A G G C C A A G G

*FIG. 1In.*

77/III

SEQ. ID. NO. 40 A G C A A C G A T C T C A G C A G C A G C C C A G  
SEQ. ID. NO. 46 T G A G C T T T G A T G A G C C T C A G A A G A A  
SEQ. ID. NO. 36 T G A G C T T T G A T G A G C C T C A G A A G A A  
SEQ. ID. NO. 32 A A G C C C G G C G G A T C A A C G A C G A G A T

SEQ. ID. NO. 40 A T G C A A G C A G A A G G T C A T C T T T G G C  
SEQ. ID. NO. 46 C G C C A T G G C C C A C G G G A A T T C T A C G  
SEQ. ID. NO. 36 C G C C A T G G C C C A C G G G A A T T C T A C G  
SEQ. ID. NO. 32 C G A G C G G C A G C T C C G C A G G G A C A A G

SEQ. ID. NO. 40 A G C G G C A C G G T C A C C T T C T C A C T G A  
SEQ. ID. NO. 46 C A C C A G A A C T C C C T G G A G G C C C A G A  
SEQ. ID. NO. 36 C A C C A G A A C T C C C T G G A G G C C C A G A  
SEQ. ID. NO. 32 C G G G A C G C C C G C C G G G A G C T C A A G C

SEQ. ID. NO. 40 G C T T T G A T G A G C C T C A G A A G A A C G C  
SEQ. ID. NO. 46 A A A G C A G C G A T A C G C T G A C C C G A C A  
SEQ. ID. NO. 36 A A A G C A G C G A T A C G C T G A C C C G A C A  
SEQ. ID. NO. 32 T G C T G C T G C T C G G G A C A G G A G A G A G

SEQ. ID. NO. 40 C A T G G C C C A C G G G A A T T C T A C G C A C  
SEQ. ID. NO. 46 C C A G C C A T T A C T C C C G C T G C A G T G C  
SEQ. ID. NO. 36 C C A G C C A T T A C T C C C G C T G C A G T G C  
SEQ. ID. NO. 32 T G G C A A G A G T A C G T T T A T C A A G C A G

SEQ. ID. NO. 40 C A G A A C T C C C T G G A G G C C C A G A A A A  
SEQ. ID. NO. 46 G G G G A A A C G G A C T T A G A T C T G A C C G  
SEQ. ID. NO. 36 G G G G A A A C G G A C T T A G A T C T G A C C G  
SEQ. ID. NO. 32 A T G A G A A T C A T C C A T G G G T C A G G A T

SEQ. ID. NO. 40 G C A G C G A T A C G C T G A C C C G A C A C C A  
SEQ. ID. NO. 46 T C C A G G A A A C A G G T C T G C A A G G A C C  
SEQ. ID. NO. 36 T C C A G G A A A C A G G T C T G C A A G G A C C  
SEQ. ID. NO. 32 A C T C T G A T G A A G A T A A A A G G G G C T T

SEQ. ID. NO. 40 G C C A T T A C T C C C G C T G C A G T G C G G G  
SEQ. ID. NO. 46 T G T G G G T G G A G A C C A G C G G C C A G A G  
SEQ. ID. NO. 36 T G T G G G T G G A G A C C A G C G G C C A G A G  
SEQ. ID. NO. 32 C A C C A A G C T G G T G T A T C A G A A C A T C

FIG. 110.

SUBSTITUTE SHEET (RULE 26)

78/III

SEQ. ID. NO. 40 G A A A C G G A C T T A G A T C T G A C C G T C C  
SEQ. ID. NO. 46 G T G G A G G A C C C T G A A G A G T T G T C C C  
SEQ. ID. NO. 36 G T G G A G G A C C C T G A A G A G T T G T C C C  
SEQ. ID. NO. 32 T T C A C G G C C A T G C A G G C C A T G A T C A

SEQ. ID. NO. 40 A G G A A A C A G G T C T G C A A G G A C C T G T  
SEQ. ID. NO. 46 C A G C A C T T G T A G T G T C C A G T T C A C A  
SEQ. ID. NO. 36 C A G C A C T T G T A G T G T C C A G T T C A C A  
SEQ. ID. NO. 32 G A G C C A T G G A C A C A C T C A A G A T C C C

SEQ. ID. NO. 40 G G G T G G A G A C C A G C G G C C A G A G G T G  
SEQ. ID. NO. 46 G A G C T T T G T C A T C A G T G G T G G A G G C  
SEQ. ID. NO. 36 G A G C T T T G T C A T C A G T G G T G G A C G C  
SEQ. ID. NO. 32 A T A C A A G T A T G A G C A C A A T A A G G C T

SEQ. ID. NO. 40 G A G G A C C C T G A A G A G T T G T C C C C A G  
SEQ. ID. NO. 46 A G C A C T G T T A C A G A A A A C G T A G T G A  
SEQ. ID. NO. 36 A G C A C T G T T A C A G A A A A C G T A G T G A  
SEQ. ID. NO. 32 C A T G C A C A A T T A G T T C G A G A A G T T G

SEQ. ID. NO. 40 C A C T T G T A G T G T C C A G T T C A C A G A G  
SEQ. ID. NO. 46 A T T C A G C G G C C G C C A T G A C T C T G G A  
SEQ. ID. NO. 36 A T T C A A T G A C T C T G G A G T C C A T C A T  
SEQ. ID. NO. 32 A T G T G G A G A A G G T G T C T G C T T T T G A

SEQ. ID. NO. 40 C T T T G T C A T C A G T G G T G G A G G C A G C  
SEQ. ID. NO. 46 G T C C A T C A T G G C G T G C T G C C T G A G C  
SEQ. ID. NO. 36 G G C G T G C T G C C T G A G C G A G G A G G C C  
SEQ. ID. NO. 32 G A A T C C A T A T G T A G A T G C A A T A A A G

SEQ. ID. NO. 40 A C T G T T A C A G A A A A C G T A G T G A A T T  
SEQ. ID. NO. 46 G A G G A G G C C A A G G A A G C C C G G C G G A  
SEQ. ID. NO. 36 A A G G A A G C C C G G C G G A T C A A C G A C G  
SEQ. ID. NO. 32 A G T T T A T G G A A T G A T C C T G G A A T C C

SEQ. ID. NO. 40 C A - - - - -  
SEQ. ID. NO. 46 T C A A C G A C G A G A T C G A G C G G C A G C T  
SEQ. ID. NO. 36 A G A T C G A G C G G C A G C T C C G C A G G G A  
SEQ. ID. NO. 32 A G G A A T G C T A T G A T A G A C G A C G A G A

*FIG. 11p.*

SUBSTITUTE SHEET (RULE 26)

79/III

SEQ. ID. NO. 40 - - - - -  
SEQ. ID. NO. 46 C C G C A G G G A C A A G C G G G A C G C C C G C  
SEQ. ID. NO. 36 C A A G C G G G A C G C C C G C C G G G A G C T C  
SEQ. ID. NO. 32 A T A T C A A T T A T C T G A C T C T A C C A A A

SEQ. ID. NO. 40 - - - - - A T G A C T C T G G  
SEQ. ID. NO. 46 C G G G A G C T C A A G C T G C T G C T G C T C G  
SEQ. ID. NO. 36 A A G C T G C T G C T G C T C G G G A C A G G A G  
SEQ. ID. NO. 32 T A C T A T C T T A A T G A C T T G G A C C G C G

SEQ. ID. NO. 40 A G T C C A T C A T G G C G T G C T G C C T G A G  
SEQ. ID. NO. 46 G G A C A G G A G A G A G T G G C A A G A G T A C  
SEQ. ID. NO. 36 A G A G T G G C A A G A G T A C G T T T A T C A A  
SEQ. ID. NO. 32 T A G C T G A C C C T G C C T A C C T G C C T A C

SEQ. ID. NO. 40 C G A G G A G G C C A A G G A A G C C C G G C G G  
SEQ. ID. NO. 46 G T T T A T C A A G C A G A T G A G A A T C A T C  
SEQ. ID. NO. 36 G C A G A T G A G A A T C A T C C A T G G G T C A  
SEQ. ID. NO. 32 G C A A C A A G A T G T G C T T A G A G T T C G A

SEQ. ID. NO. 40 A T C A A C G A C G A G A T C G A G C G G C A G C  
SEQ. ID. NO. 46 C A T G G G T C A G G A T A C T C T G A T G A A G  
SEQ. ID. NO. 36 G G A T A C T C T G A T G A A G A T A A A A G G G  
SEQ. ID. NO. 32 G T C C C C A C C A C A G G G A T C A T C G A A T

SEQ. ID. NO. 40 T C C G C A G G G A C A A G C G G G A C G C C C G  
SEQ. ID. NO. 46 A T A A A A G G G G C T T C A C C A A G C T G G T  
SEQ. ID. NO. 36 G C T T C A C C A A G C T G G T G T A T C A G A A  
SEQ. ID. NO. 32 A C C C C T T T G A C T T A C A A A G T G T C A T

SEQ. ID. NO. 40 C C G G G A G C T C A A G C T G C T G C T G C T C  
SEQ. ID. NO. 46 G T A T C A G A A C A T C T T C A C G G C C A T G  
SEQ. ID. NO. 36 C A T C T T C A C G G C C A T G C A G G C C A T G  
SEQ. ID. NO. 32 T T T C A G A A T G G T C G A T G T A G G G G G C

SEQ. ID. NO. 40 G G G A C A G G A G A G A G T G G C A A G A G T A  
SEQ. ID. NO. 46 C A G G C C A T G A T C A G A G C C A T G G A C A  
SEQ. ID. NO. 36 A T C A G A G C C A T G G A C A C A C T C A A G A  
SEQ. ID. NO. 32 C A A A G G T C A G A G A G A A G A A A A T G G A

*FIG. 11q.*

SUBSTITUTE SHEET (RULE 26)

80/III

SEQ. ID. NO. 40 C G T T T A T C A A G C A G A T G A G A A T C A T  
SEQ. ID. NO. 46 C A C T C A A G A T C C C A T A C A A G T A T G A  
SEQ. ID. NO. 36 T C C C A T A C A A G T A T G A G C A C A A T A A  
SEQ. ID. NO. 32 T A C A C T G C T T T G A A A A T G T C A C C T C

SEQ. ID. NO. 40 C C A T G G G T C A G G A T A C T C T G A T G A A  
SEQ. ID. NO. 46 G C A C A A T A A G G C T C A T G C A C A A T T A  
SEQ. ID. NO. 36 G G C T C A T G C A C A A T T A G T T C G A G A A  
SEQ. ID. NO. 32 T A T C A T G T T T C T A G T A G C G C T T A G T

SEQ. ID. NO. 40 G A T A A A A G G G G C T T C A C C A A G C T G G  
SEQ. ID. NO. 46 G T T C G A G A A G T T G A T G T G G A G A A G G  
SEQ. ID. NO. 36 G T T G A T G T G G A G A A G G T G T C T G C T T  
SEQ. ID. NO. 32 G A A T A T G A T C A A G T T C T C G T G G A G T

SEQ. ID. NO. 40 T G T A T C A G A A C A T C T T C A C G G C C A T  
SEQ. ID. NO. 46 T G T C T G C T T T T G A G A A T C C A T A T G T  
SEQ. ID. NO. 36 T T G A G A A T C C A T A T G T A G A T G C A A T  
SEQ. ID. NO. 32 C A G A C A A T G A G A A C C G A A T G G A G G A

SEQ. ID. NO. 40 G C A G G C C A T G A T C A G A G C C A T G G A C  
SEQ. ID. NO. 46 A G A T G C A A T A A A G A G T T T A T G G A A T  
SEQ. ID. NO. 36 A A A G A G T T T A T G G A A T G A T C C T G G A  
SEQ. ID. NO. 32 A A G C A A G G C T C T C T T T A G A A C A A T T

SEQ. ID. NO. 40 A C A C T C A A G A T C C C A T A C A A G T A T G  
SEQ. ID. NO. 46 G A T C C T G G A A T C C A G G A A T G C T A T G  
SEQ. ID. NO. 36 A T C C A G G A A T G C T A T G A T A G A C G A C  
SEQ. ID. NO. 32 A T C A C A T A C C C C T G G T T C C A G A A C T

SEQ. ID. NO. 40 A G C A C A A T A A G G C T C A T G C A C A A T T  
SEQ. ID. NO. 46 A T A G A C G A C G A G A A T A T C A A T T A T C  
SEQ. ID. NO. 36 G A G A A T A T C A A T T A T C T G A C T C T A C  
SEQ. ID. NO. 32 C C T C G G T T A T T C T G T T C T T A A A C A A

SEQ. ID. NO. 40 A G T T C G A G A A G T T G A T G T G G A G A A G  
SEQ. ID. NO. 46 T G A C T C T A C C A A A T A C T A T C T T A A T  
SEQ. ID. NO. 36 C A A A T A C T A T C T T A A T G A C T T G G A C  
SEQ. ID. NO. 32 G A A A G A T C T T C T A G A G G A G A A A A T C

*FIG. 1/r.*



81/III

SEQ. ID. NO. 40 G T G T C T G C T T T T G A G A A T C C A T A T G  
SEQ. ID. NO. 46 G A C T T G G A C C G C G T A G C T G A C C C T G  
SEQ. ID. NO. 36 C G C G T A G C T G A C C C T G C C T A C C T G C  
SEQ. ID. NO. 32 A T G T A T T C C C A T C T A G T C G A C T A C T

SEQ. ID. NO. 40 T A G A T G C A A T A A A G A G T T T A T G G A A  
SEQ. ID. NO. 46 C C T A C C T G C C T A C G C A A C A A G A T G T  
SEQ. ID. NO. 36 C T A C G C A A C A A G A T G T G C T T A G A G T  
SEQ. ID. NO. 32 T C C C A G A A T A T G A T G G A C C C C A G A G

SEQ. ID. NO. 40 T G A T C C T G G A A T C C A G G A A T G C T A T  
SEQ. ID. NO. 46 G C T T A G A G T T C G A G T C C C C A C C A C A  
SEQ. ID. NO. 36 T C G A G T C C C C A C C A C A G G G A T C A T C  
SEQ. ID. NO. 32 A G A T G C C C A G G C A G C C C G A G A A T T C

SEQ. ID. NO. 40 G A T A G A C G A C G A G A A T A T C A A T T A T  
SEQ. ID. NO. 46 G G G A T C A T C G A A T A C C C C T T T G A C T  
SEQ. ID. NO. 36 G A A T A C C C C T T T G A C T T A C A A A G T G  
SEQ. ID. NO. 32 A T T C T G A A G A T G T T C G T G G A C C T G A

SEQ. ID. NO. 40 C T G A C T C T A C C A A A T A C T A T C T T A A  
SEQ. ID. NO. 46 T A C A A A G T G T C A T T T T C A G A A T G G T  
SEQ. ID. NO. 36 T C A T T T T C A G A A T G G T C G A T G T A G G  
SEQ. ID. NO. 32 A C C C A G A C A G T G A C A A A A T T A T C T A

SEQ. ID. NO. 40 T G A C T T G G A C C G C G T A G C T G A C C C T  
SEQ. ID. NO. 46 C G A T G T A G G G G G C C A A A G G T C A G A G  
SEQ. ID. NO. 36 G G G C C A A A G G T C A G A G A G A A G A A A A  
SEQ. ID. NO. 32 C T C C C A C T T C A C G T G C G C C A C A G A C

SEQ. ID. NO. 40 G C C T A C C T G C C T A C G C A A C A A G A T G  
SEQ. ID. NO. 46 A G A A G A A A A T G G A T A C A C T G C T T T G  
SEQ. ID. NO. 36 T G G A T A C A C T G C T T T G A A A A T G T C A  
SEQ. ID. NO. 32 A C C G A G A A T A T C C G C T T T G T C T T T G

SEQ. ID. NO. 40 T G C T T A G A G T T C G A G T C C C C A C C A C  
SEQ. ID. NO. 46 A A A A T G T C A C C T C T A T C A T G T T T C T  
SEQ. ID. NO. 36 C C T C T A T C A T G T T T C T A G T A G C G C T  
SEQ. ID. NO. 32 C T G C C G T C A A G G A C A C C A T C C T C C A

FIG. 1/Is.

SUBSTITUTE SHEET (RULE 26)

82/III

SEQ. ID. NO. 40 A G G G A T C A T C G A A T A C C C C T T T G A C  
SEQ. ID. NO. 46 A G T A G C G C T T A G T G A A T A T G A T C A A  
SEQ. ID. NO. 36 T A G T G A A T A T G A T C A A G T T C T C G T G  
SEQ. ID. NO. 32 G T T G A A C C T G A A G G A C T G C G G T C T G

SEQ. ID. NO. 40 T T A C A A A G T G T C A T T T T C A G A A T G G  
SEQ. ID. NO. 46 G T T C T C G T G G A G T C A G A C A A T G A G A  
SEQ. ID. NO. 36 G A G T C A G A C A A T G A G A A C C G A A T G G  
SEQ. ID. NO. 32 T T C T A A

SEQ. ID. NO. 40 T C G A T G T A G G G G G C C A A A G G T C A G A  
SEQ. ID. NO. 46 A C C G A A T G G A G G A A A G C A A G G C T C T  
SEQ. ID. NO. 36 A G G A A A G C A A G G C T C T C T T T A G A A C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A G A A G A A A A T G G A T A C A C T G C T T T  
SEQ. ID. NO. 46 C T T T A G A A C A A T T A T C A C A T A C C C C  
SEQ. ID. NO. 36 A A T T A T C A C A T A C C C C T G G T T C C A G  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A A A A T G T C A C C T C T A T C A T G T T T C  
SEQ. ID. NO. 46 T G G T T C C A G A A C T C C T C G G T T A T T C  
SEQ. ID. NO. 36 A A C T C C T C G G T T A T T C T G T T C T T A A  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T A G T A G C G C T T A G T G A A T A T G A T C A  
SEQ. ID. NO. 46 T G T T C T T A A A C A A G A A A G A T C T T C T  
SEQ. ID. NO. 36 A C A A G A A A G A T C T T C T A G A G G A G A A  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A G T T C T C G T G G A G T C A G A C A A T G A G  
SEQ. ID. NO. 46 A G A G G A G A A A A T C A T G T A T T C C C A T  
SEQ. ID. NO. 36 A A T C A T G T A T T C C C A T C T A G T C G A C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A A C C G A A T G G A G G A A A G C A A G G C T C  
SEQ. ID. NO. 46 C T A G T C G A C T A C T T C C C A G A A T A T G  
SEQ. ID. NO. 36 T A C T T C C C A G A A T A T G A T G G A C C C C  
SEQ. ID. NO. 32

*FIG. 11.*

SUBSTITUTE SHEET (RULE 26)

83/III

SEQ. ID. NO. 40 T C T T T A G A A C A A T T A T C A C A T A C C C  
SEQ. ID. NO. 46 A T G G A C C C C A G A G A G A T G C C C A G G C  
SEQ. ID. NO. 36 A G A G A G A T G C C C A G G C A G C C C G A G A  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C T G G T T C C A G A A C T C C T C G G T T A T T  
SEQ. ID. NO. 46 A G C C C G A G A A T T C A T T C T G A A G A T G  
SEQ. ID. NO. 36 A T T C A T T C T G A A G A T G T T C G T G G A C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C T G T T C T T A A A C A A G A A A G A T C T T C  
SEQ. ID. NO. 46 T T C G T G G A C C T G A A C C C A G A C A G T G  
SEQ. ID. NO. 36 C T G A A C C C A G A C A G T G A C A A A A T T A  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T A G A G G A G A A A A T C A T G T A T T C C C A  
SEQ. ID. NO. 46 A C A A A A T T A T C T A C T C C C A C T T C A C  
SEQ. ID. NO. 36 T C T A C T C C C A C T T C A C G T G C G C C A C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 T C T A G T C G A C T A C T T C C C A G A A T A T  
SEQ. ID. NO. 46 G T G C G C C A C A G A C A C C G A G A A T A T C  
SEQ. ID. NO. 36 A G A C A C C G A G A A T A T C C G C T T T G T C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A T G G A C C C C A G A G A G A T G C C C A G G  
SEQ. ID. NO. 46 C G C T T T G T C T T T G C T G C C G T C A A G G  
SEQ. ID. NO. 36 T T T G C T G C C G T C A A G G A C A C C A T C C  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C A G C C C G A G A A T T C A T T C T G A A G A T  
SEQ. ID. NO. 46 A C A C C A T C C T C C A G T T G A A C C T G A A  
SEQ. ID. NO. 36 T C C A G T T G A A C C T G A A G G A C T G C G G  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G T T C G T G G A C C T G A A C C C A G A C A G T  
SEQ. ID. NO. 46 G G A C T G C G G T C T G T T C T A A T T G T G C  
SEQ. ID. NO. 36 T C T G T T C T A A  
SEQ. ID. NO. 32

FIG. 11u.

SUBSTITUTE SHEET (RULE 26)

84/III

SEQ. ID. NO. 40 G A C A A A A T T A T C T A C T C C C A C T T C A  
SEQ. ID. NO. 46 C T C C T A G A C A C C C G C C C T G C C C T T C  
SEQ. ID. NO. 36  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C G T G C G C C A C A G A C A C C G A G A A T A T  
SEQ. ID. NO. 46 C C T G G T  
SEQ. ID. NO. 36  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 C C G C T T T G T C T T T G C T G C C G T C A A G  
SEQ. ID. NO. 46  
SEQ. ID. NO. 36  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 G A C A C C A T C C T C C A G T T G A A C C T G A  
SEQ. ID. NO. 46  
SEQ. ID. NO. 36  
SEQ. ID. NO. 32

SEQ. ID. NO. 40 A G G A C T G C G G T C T G T T C T A A  
SEQ. ID. NO. 46  
SEQ. ID. NO. 36  
SEQ. ID. NO. 32

*FIG. 1/iv.*

85/III

**ClustalW Formatted Alignments**

SEQ. ID. NO. 41 M V C E G K R S A S C P C F F L L T A K F Y W I L  
 SEQ. ID. NO. 47 M G S L L A L P A L L L L W G A V A E G P A K K V  
 SEQ. ID. NO. 37 M G S L L A L P A L L L L W G A V A E G P A K K V  
 SEQ. ID. NO. 33 M A F Y S C C W V L L A L T W H T S A Y G P D Q R

SEQ. ID. NO. 41 T M M Q R T H S Q E Y A H S I R V D G D I I L G G  
 SEQ. ID. NO. 47 L T L E G D L V L G G L F P V H Q K G G P A E D C  
 SEQ. ID. NO. 37 L T L E G D L V L G G L F P V H Q K G G P A E D C  
 SEQ. ID. NO. 33 A Q K K G D I I L G G L F P I H F G V A A K D Q D

SEQ. ID. NO. 41 L F P V H A K G E R G V P C G E L K K E K G I H R  
 SEQ. ID. NO. 47 G P V N E H R G I Q R L E A M L F A L D R I N R D  
 SEQ. ID. NO. 37 G P V N E H R G I Q R L E A M L F A L D R I N R D  
 SEQ. ID. NO. 33 L K S R P E S V E C I R Y N F R G F R W L Q A M I

SEQ. ID. NO. 41 L E A M L Y A I D Q I N K D P D L L S N I T L G V  
 SEQ. ID. NO. 47 P H L L P G V R L G A H I L D S C S K D T H A L E  
 SEQ. ID. NO. 37 P H L L P G V R L G A H I L D S C S K D T H A L E  
 SEQ. ID. NO. 33 F A I E E I N S S P A L L P N L T L G Y R I F D T

SEQ. ID. NO. 41 R I L D T C S R D T Y A L E Q S L T F V Q A L I E  
 SEQ. ID. NO. 47 Q A L D F V R A S L S R G A D G S R H I C P D G S  
 SEQ. ID. NO. 37 Q A L D F V R A S L S R G A D G S R H I C P D G S  
 SEQ. ID. NO. 33 C N T V S K A L E A T L S F V A Q N K I D S L N L

SEQ. ID. NO. 41 K D A S D V K C A N G D P P I F T K P D K I S G V  
 SEQ. ID. NO. 47 Y A T H G D A P T A I T G V I G G S Y S D V S I Q  
 SEQ. ID. NO. 37 Y A T H G D A P T A I T G V I G G S Y S D V S I Q  
 SEQ. ID. NO. 33 D E F C N C S E H I P S T I A V V G A T G S G V S

SEQ. ID. NO. 41 I G A A A S S V S I M V A N I L R L F K I P Q I S  
 SEQ. ID. NO. 47 V A N L L R L F Q I P Q I S Y A S T S A K L S D K  
 SEQ. ID. NO. 37 V A N L L R L F Q I P Q I S Y A S T S A K L S D K  
 SEQ. ID. NO. 33 T A V A N L L G L F Y I P Q V S Y A S S S R L L S

SEQ. ID. NO. 41 Y A S T A P E L S D N T R Y D F F S R V V P P D S  
 SEQ. ID. NO. 47 S R Y D Y F A R T V P P D F F Q A K A M A E I L R  
 SEQ. ID. NO. 37 S R Y D Y F A R T V P P D F F Q A K A M A E I L R  
 SEQ. ID. NO. 33 N K N Q F K S F L R T I P N D E H Q A T A M A D I

*FIG. 12a.*

SUBSTITUTE SHEET (RULE 26)

86/III

SEQ. ID. NO. 41 YQAQAMVDIVTALGWNYVSTLASEG  
 SEQ. ID. NO. 47 FFNWTYVSTVASEGDYGETGIEAFE  
 SEQ. ID. NO. 37 FFNWTYVSTVASEGDYGETGIEAFE  
 SEQ. ID. NO. 33 IEYFRWNWVGTTAAADDDYGRPGIEK

SEQ. ID. NO. 41 NYGESGVEAFTQISREIGGVCIAQS  
 SEQ. ID. NO. 47 LEARARNICVATSEKVGGRAMSRAAF  
 SEQ. ID. NO. 37 LEARARNICVATSEKVGGRAMSRAAF  
 SEQ. ID. NO. 33 FREEAEERDIDFSELISQYSDEE

SEQ. ID. NO. 41 QKIPREPRPGEFEKI IKRLLET PNA  
 SEQ. ID. NO. 47 EGVVRALLQKPSARVAVLFT RSEDA  
 SEQ. ID. NO. 37 EGVVRALLQKPSARVAVLFT RSEDA  
 SEQ. ID. NO. 33 EIQHVVEVIQNSTAKVIVVFSSGPD

SEQ. ID. NO. 41 RAVIMFANEDDIRRI LEAAKKLNQS  
 SEQ. ID. NO. 47 REL LAASQRLNASFTWVASD GWGAL  
 SEQ. ID. NO. 37 REL LAASQRLNASFTWVASD GWGAL  
 SEQ. ID. NO. 33 LEPLIKEIVRRNITGKIWLASEAWA

SEQ. ID. NO. 41 GHFLWIGSDSWGSKIAPVYQQEEIA  
 SEQ. ID. NO. 47 ESVVAGSEGA AEGAITIELASYPIS  
 SEQ. ID. NO. 37 ESVVAGSEGA AEGAITIELASYPIS  
 SEQ. ID. NO. 33 SSSLIAM PQYFHVVG GTIGFALKAG

SEQ. ID. NO. 41 EGAVTILPKRASIDGFDRYFRSRTL  
 SEQ. ID. NO. 47 DFASYFQSLDPWNNSRNPWFREFWE  
 SEQ. ID. NO. 37 DFASYFQSLDPWNNSRNPWFREFWE  
 SEQ. ID. NO. 33 QIPGFRREFLKKVHPRKSVHNGFAKE

SEQ. ID. NO. 41 ANNRRNVWF AEFW EENFGCKLGSHG  
 SEQ. ID. NO. 47 QRFRC SFRQRDCAAHSLRAVPFEQE  
 SEQ. ID. NO. 37 QRFRC SFRQRDCAAHSLRAVPFEQE  
 SEQ. ID. NO. 33 FWEETFNCHLQEGAKGPLPVDTFLR

SEQ. ID. NO. 41 KRNSHIKKCTGLERIARDSSSYEQEG  
 SEQ. ID. NO. 47 SKIMFVVNAVYAMAHALHNMHRA LC  
 SEQ. ID. NO. 37 SKIMFVVNAVYAMAHALHNMHRA LC  
 SEQ. ID. NO. 33 GHEESGDRFSNSSTAFRPLCTG DEN

FIG. 12b.

87/III

SEQ. ID. NO. 41 K V Q F V I D A V Y S M A Y A L H N M H K D L C P  
 SEQ. ID. NO. 47 P N T T R L C D A M R P V N G R R L Y K D F V L N  
 SEQ. ID. NO. 37 P N T T R L C D A M R P V N G R R L Y K D F V L N  
 SEQ. ID. NO. 33 I S S V E T P Y I D Y T H L R I S Y N V Y L A V Y

SEQ. ID. NO. 41 G Y I G L C P R M S T I D G K E L L G Y I R A V N  
 SEQ. ID. NO. 47 V K F D A P F R P A D T H N E V R F D R F G D G I  
 SEQ. ID. NO. 37 V K F D A P F R P A D T H N E V R F D R F G D G I  
 SEQ. ID. NO. 33 S I A H A L Q D I Y T C L P G R G L F T N G S C A

SEQ. ID. NO. 41 F N G S A G T P V T F N E N G D A P G R Y D I F Q  
 SEQ. ID. NO. 47 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A  
 SEQ. ID. NO. 37 G R Y N I F T Y L R A G S G R Y R Y Q K V G Y W A  
 SEQ. ID. NO. 33 D I K K V E A W Q V L K H L R H L N F T N N M G E

SEQ. ID. NO. 41 Y Q I T N K S T E Y K V I G H W T N Q L H L K V E  
 SEQ. ID. NO. 47 E G L T L D T S L I P W A S P S A G P L P A S R C  
 SEQ. ID. NO. 37 E G L T L D T S L I P W A S P S A G P L P A S R C  
 SEQ. ID. NO. 33 Q V T F D E C G D L V G N Y S I I N W H L S P E D

SEQ. ID. NO. 41 D M Q W A H R E H T H P A S V C S L P C K P G E R  
 SEQ. ID. NO. 47 S E P C L Q N E V K S V Q P G E V C C W L C I P C  
 SEQ. ID. NO. 37 S E P C L Q N E V K S V Q P G E V C C W L C I P C  
 SEQ. ID. NO. 33 G S I V F K E V G Y Y N V Y A K K G E R L F I N E

SEQ. ID. NO. 41 K K T V K G V P C C W H C E R C E G Y N Y Q V D E  
 SEQ. ID. NO. 47 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L  
 SEQ. ID. NO. 37 Q P Y E Y R L D E F T C A D C G L G Y W P N A S L  
 SEQ. ID. NO. 33 E K I L W S G F S R E V P F S N C S R D C L A G T

SEQ. ID. NO. 41 L S C E L C P L D Q R P N M N R T G C Q L I P I I  
 SEQ. ID. NO. 47 T G C F E L P Q E Y I R W G D A W A V G P V T I A  
 SEQ. ID. NO. 37 T G C F E L P Q E Y I R W G D A W A V G P V T I A  
 SEQ. ID. NO. 33 R K G I I E G E P T C C F E C V E C P D G E Y S D

SEQ. ID. NO. 41 K L E W H S P W A V V P V F V A I L G I I A T T F  
 SEQ. ID. NO. 47 C L G A L A T L F V L G V F V R H N A T P V V K A  
 SEQ. ID. NO. 37 C L G A L A T L F V L G V F V R H N A T P V V K A  
 SEQ. ID. NO. 33 E T D A S A C N K C P D D F W S N E N H T S C F E

FIG. 12c.

SUBSTITUTE SHEET (RULE 26)

88/III

SEQ. ID. NO. 41 V I V T F V R Y N D T P I V R A S G R E L S Y V L  
 SEQ. ID. NO. 47 S G R E L C Y I L L G G V F L C Y C M T F I F I A  
 SEQ. ID. NO. 37 S G R E L C Y I L L G G V F L C Y C M T F I F I A  
 SEQ. ID. NO. 33 L P Q E Y I R W G D A W A V G P V T I A C L G A L

SEQ. ID. NO. 41 L T G I F L C Y S I T F L M I A A P D T I I C S F  
 SEQ. ID. NO. 47 K P S T A V C T L R R L G L G T A F S V C Y S A L  
 SEQ. ID. NO. 37 K P S T A V C T L R R L G L G T A F S V C Y S A L  
 SEQ. ID. NO. 33 A T L F V L G V F V R H N A T P V V K A S G R E L

SEQ. ID. NO. 41 R R V F L G L G M C F S Y A A L L T K T N R I H R  
 SEQ. ID. NO. 47 L T K T N R I A R I F G G A R E G A Q R P R F I S  
 SEQ. ID. NO. 37 L T K T N R I A R I F G G A R E G A Q R P R F I S  
 SEQ. ID. NO. 33 C Y I L L G G V F L C Y C M T F I F I A K P S T A

SEQ. ID. NO. 41 I F E Q G K K S V T A P K F I S P A S Q L V I T F  
 SEQ. ID. NO. 47 P A S Q V A I C L A L I S G Q L L I V V A W L V V  
 SEQ. ID. NO. 37 P A S Q V A I C L A L I S G Q L L I V V A W L V V  
 SEQ. ID. NO. 33 V C T L R R L G L G T A F S V C Y S A L L T K T N

SEQ. ID. NO. 41 S L I S V Q L L G V F V W F V V D P P H I I I D Y  
 SEQ. ID. NO. 47 E A P G T G K E T A P E R R E V V T L R C N H R D  
 SEQ. ID. NO. 37 E A P G T G K E T A P E R R E V V T L R C N H R D  
 SEQ. ID. NO. 33 R I A R I F G G A R E G A Q R P R F I S P A S Q V

SEQ. ID. NO. 41 G E Q R T L D P E K A R G V L K C D I S D L S L I  
 SEQ. ID. NO. 47 A S M L G S L A Y N V L L I A L C T L Y A F K T R  
 SEQ. ID. NO. 37 A S M L G S L A Y N V L L I A L C T L Y A F K T R  
 SEQ. ID. NO. 33 A I C L A L I S G Q L L I V V A W L V V E A P G T

SEQ. ID. NO. 41 C S L G Y S I L L M V T C T V Y A I K T R G V P E  
 SEQ. ID. NO. 47 K C P E N F N E A K F I G F T M Y T T C I I W L A  
 SEQ. ID. NO. 37 K C P E N F N E A K F I G F T M Y T T C I I W L A  
 SEQ. ID. NO. 33 G K E T A P E R R E V V T L R C N H R D A S M L G

SEQ. ID. NO. 41 T F N E A K P I G F T M Y T T C I I W L A F I P I  
 SEQ. ID. NO. 47 F L P I F Y V T S S D Y R V Q T T T M C V S V S L  
 SEQ. ID. NO. 37 F L P I F Y V T S S D Y R V Q T T T M C V S V S L  
 SEQ. ID. NO. 33 S L A Y N V L L I A L C T L Y A F N T R K C P E N

FIG. 12d.

SUBSTITUTE SHEET (RULE 26)



89/III

SEQ. ID. NO. 41 F F G T A Q S A E K M Y I Q T T T L T V S M S L S  
 SEQ. ID. NO. 47 S G S V V L G C L F A P K L H I I L F Q P Q K N T  
 SEQ. ID. NO. 37 S G S V V L G C L F A P K L H I I L F Q P Q K N T  
 SEQ. ID. NO. 33 F N E A K F I G F T M Y T T C I I W L A L L P I F

SEQ. ID. NO. 41 A S V S L G M L Y M P K V Y I I I F H P E Q N T I  
 SEQ. ID. NO. 47 I E E V R C S T A A H A F K V A A R A T L R R S N  
 SEQ. ID. NO. 37 I E E V R C S T A A H A F K V A A R A T L R R S N  
 SEQ. ID. NO. 33 Y V T S S D Y R V Q T T T M C V S V S L S G S V V

SEQ. ID. NO. 41 E E V R C S T A A H A F K V A A R A T L R R S N V  
 SEQ. ID. NO. 47 V S R K R S S S L G G S T G S T P S S S I S S K S  
 SEQ. ID. NO. 37 V S R K R S S S L G G S T G S T P S S S I S S K S  
 SEQ. ID. NO. 33 L G C L F A P K L H I I L F Q P Q K N V V S H R A

SEQ. ID. NO. 41 S R K R S S S L G G S T G S T P S S S I S S K S N  
 SEQ. ID. NO. 47 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q  
 SEQ. ID. NO. 37 N S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q  
 SEQ. ID. NO. 33 P T S R F G S A A A R A S S S L G Q G S G S Q F V

SEQ. ID. NO. 41 S E D P F P Q P E R Q K Q Q Q P L A L T Q Q E Q Q  
 SEQ. ID. NO. 47 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F  
 SEQ. ID. NO. 37 Q Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F  
 SEQ. ID. NO. 33 P T V C N G R E V V D S T T S S L M T L E S I M A

SEQ. ID. NO. 41 Q Q P L T L P Q Q Q R S Q Q Q P R C K Q K V I F G  
 SEQ. ID. NO. 47 G S G T V T F S L S F D E P Q K N A M A H G N S T  
 SEQ. ID. NO. 37 G S G T V T F S L S F D E P Q K N A M A H G N S T  
 SEQ. ID. NO. 33 C C L S E E A K E A R R I N D E I E R Q L R R D K

SEQ. ID. NO. 41 S G T V T F S L S F D E P Q K N A M A H G N S T H  
 SEQ. ID. NO. 47 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C  
 SEQ. ID. NO. 37 H Q N S L E A Q K S S D T L T R H Q P L L P L Q C  
 SEQ. ID. NO. 33 R D A R R E L K L L L L G T G E S G K S T F I K Q

SEQ. ID. NO. 41 Q N S L E A Q K S S D T L T R H Q P L L P L Q C G  
 SEQ. ID. NO. 47 G E T D L D L T V Q E T G L Q G P V G G D Q R P E  
 SEQ. ID. NO. 37 G E T D L D L T V Q E T G L Q G P V G G D Q R P E  
 SEQ. ID. NO. 33 M R I I H G S G Y S D E D K R G F T K L V Y Q N I

FIG. 12e.

SUBSTITUTE SHEET (RULE 26)

90/III

SEQ. ID. NO. 41 E T D L D L T V Q E T G L Q G P V G G D Q R P E V  
 SEQ. ID. NO. 47 V E D P E E L S P A L V V S S S Q S F V I S G G G  
 SEQ. ID. NO. 37 V E D P E E L S P A L V V S S S Q S F V I S G G G  
 SEQ. ID. NO. 33 F T A M Q A M I R A M D T L K I P Y K Y E H N K A

SEQ. ID. NO. 41 E D P E E L S P A L V V S S S Q S F V I S G G G S  
 SEQ. ID. NO. 47 S T V T E N V V N S A A A M T L E S I M A C C L S  
 SEQ. ID. NO. 37 S T V T E N V V N S M T L E S I M A C C L S E E A  
 SEQ. ID. NO. 33 H A Q L V R E V D V E K V S A F E N P Y V D A I K

SEQ. ID. NO. 41 T V T E N V V N S M T L E S I M A C C L S E E A K  
 SEQ. ID. NO. 47 E E A K E A R R I N D E I E R Q L R R D K R D A R  
 SEQ. ID. NO. 37 K E A R R I N D E I E R Q L R R D K R D A R R E L  
 SEQ. ID. NO. 33 S L W N D P G I Q E C Y D R R R E Y Q L S D S T K

SEQ. ID. NO. 41 E A R R I N D E I E R Q L R R D K R D A R R E L K  
 SEQ. ID. NO. 47 R E L K L L L L G T G E S G K S T F I K Q M R I I  
 SEQ. ID. NO. 37 K L L L L G T G E S G K S T F I K Q M R I I H G S  
 SEQ. ID. NO. 33 Y Y L N D L D R V A D P A Y L P T Q Q D V L R V R

SEQ. ID. NO. 41 L L L L G T G E S G K S T F I K Q M R I I H G S G  
 SEQ. ID. NO. 47 H G S G Y S D E D K R G F T K L V Y Q N I F T A M  
 SEQ. ID. NO. 37 G Y S D E D K R G F T K L V Y Q N I F T A M Q A M  
 SEQ. ID. NO. 33 V P T T G I I E Y P F D L Q S V I F R M V D V G G

SEQ. ID. NO. 41 Y S D E D K R G F T K L V Y Q N I F T A M Q A M I  
 SEQ. ID. NO. 47 Q A M I R A M D T L K I P Y K Y E H N K A H A Q L  
 SEQ. ID. NO. 37 I R A M D T L K I P Y K Y E H N K A H A Q L V R E  
 SEQ. ID. NO. 33 Q R S E R R K W I H C F E N V T S I M F L V A L S

SEQ. ID. NO. 41 R A M D T L K I P Y K Y E H N K A H A Q L V R E V  
 SEQ. ID. NO. 47 V R E V D V E K V S A F E N P Y V D A I K S L W N  
 SEQ. ID. NO. 37 V D V E K V S A F E N P Y V D A I K S L W N D P G  
 SEQ. ID. NO. 33 E Y D Q V L V E S D N E N R M E E S K A L F R T I

SEQ. ID. NO. 41 D V E K V S A F E N P Y V D A I K S L W N D P G I  
 SEQ. ID. NO. 47 D P G I Q E C Y D R R R E Y Q L S D S T K Y Y L N  
 SEQ. ID. NO. 37 I Q E C Y D R R R E Y Q L S D S T K Y Y L N D L D  
 SEQ. ID. NO. 33 I T Y P W F Q N S S V I L F L N K K D L L E E K I

FIG. 12f.

SUBSTITUTE SHEET (RULE 26)

91/III

SEQ. ID. NO. 41 Q E C Y D R R R E Y Q L S D S T K Y Y L N D L D R  
 SEQ. ID. NO. 47 D L D R V A D P A Y L P T Q Q D V L R V R V P T T  
 SEQ. ID. NO. 37 R V A D P A Y L P T Q Q D V L R V R V P T T G I I  
 SEQ. ID. NO. 33 M Y S H L V D Y F P E Y D G P Q R D A Q A A R E F

SEQ. ID. NO. 41 V A D P A Y L P T Q Q D V L R V R V P T T G I I E  
 SEQ. ID. NO. 47 G I I E Y P F D L Q S V I F R M V D V G G Q R S E  
 SEQ. ID. NO. 37 E Y P F D L Q S V I F R M V D V G G Q R S E R R K  
 SEQ. ID. NO. 33 I L K M F V D L N P D S D K I I Y S H F T C A T D

SEQ. ID. NO. 41 Y P F D L Q S V I F R M V D V G G Q R S E R R K W  
 SEQ. ID. NO. 47 R R K W I H C F E N V T S I M F L V A L S E Y D Q  
 SEQ. ID. NO. 37 W I H C F E N V T S I M F L V A L S E Y D Q V L V  
 SEQ. ID. NO. 33 T E N I R F V F A A V K D T I L Q L N L K D C G L

SEQ. ID. NO. 41 I H C F E N V T S I M F L V A L S E Y D Q V L V E  
 SEQ. ID. NO. 47 V L V E S D N E N R M E E S K A L F R T I I T Y P  
 SEQ. ID. NO. 37 E S D N E N R M E E S K A L F R T I I T Y P W F Q  
 SEQ. ID. NO. 33 F

SEQ. ID. NO. 41 S D N E N R M E E S K A L F R T I I T Y P W F Q N  
 SEQ. ID. NO. 47 W F Q N S S V I L F L N K K D L L E E K I M Y S H  
 SEQ. ID. NO. 37 N S S V I L F L N K K D L L E E K I M Y S H L V D  
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 S S V I L F L N K K D L L E E K I M Y S H L V D Y  
 SEQ. ID. NO. 47 L V D Y F P E Y D G P Q R D A Q A A R E F I L K M  
 SEQ. ID. NO. 37 Y F P E Y D G P Q R D A Q A A R E F I L K M F V D  
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 F P E Y D G P Q R D A Q A A R E F I L K M F V D L  
 SEQ. ID. NO. 47 F V D L N P D S D K I I Y S H F T C A T D T E N I  
 SEQ. ID. NO. 37 L N P D S D K I I Y S H F T C A T D T E N I R F V  
 SEQ. ID. NO. 33

SEQ. ID. NO. 41 N P D S D K I I Y S H F T C A T D T E N I R F V F  
 SEQ. ID. NO. 47 R F V F A A V K D T I L Q L N L K D C G L F  
 SEQ. ID. NO. 37 F A A V K D T I L Q L N L K D C G L F  
 SEQ. ID. NO. 33

FIG. 12g.

SUBSTITUTE SHEET (RULE 26)

92/III

SEQ. ID. NO. 41 A A V K D T I L Q L N L K D C G L F  
SEQ. ID. NO. 47  
SEQ. ID. NO. 37  
SEQ. ID. NO. 33

*FIG. 12h.*

93/III

**ClustalW Formatted Alignments**

SEQ. ID. NO. 44 A T G T T G C T G C T G C T G C T A C T G G C G C  
SEQ. ID. NO. 42 A T G G C T T C C C C G C G G A G C T C C G G G C

SEQ. ID. NO. 44 C A C T C T T C C T C C G C C C C C C G G G C G C  
SEQ. ID. NO. 42 A G C C C G G G C C G C C G C C G C C G C C G C C

SEQ. ID. NO. 44 G G G C G G G G C G C A G A C C C C C A A C G C C  
SEQ. ID. NO. 42 A C C G C C G C C C G C G C G C C T G C T A C T G

SEQ. ID. NO. 44 A C C T C A G A A G G T T G C C A G A T C A T A C  
SEQ. ID. NO. 42 C T A C T G C T G C T G C C G C T G C T G C T G C

SEQ. ID. NO. 44 A C C C G C C C T G G G A A G G G G G C A T C A G  
SEQ. ID. NO. 42 C T C T G G C G C C C G G G G C C T G G G G C T G

SEQ. ID. NO. 44 G T A C C G G G G C C T G A C T C G G G A C C A G  
SEQ. ID. NO. 42 G G C G C G G G G C G C C C C C C G G C C G C C G

SEQ. ID. NO. 44 G T G A A G G C T A T C A A C T T C C T G C C A G  
SEQ. ID. NO. 42 C C C A G C A G C C C G C C G C T C T C C A T C A

SEQ. ID. NO. 44 T G G A C T A T G A G A T T G A G T A T G T G T G  
SEQ. ID. NO. 42 T G G G C C T C A T G C C G C T C A C C A A G G A

SEQ. ID. NO. 44 C C G G G G G G A G C G C G A G G T G G T G G G G  
SEQ. ID. NO. 42 G G T G G C C A A G G G C A G C A T C G G G C G C

SEQ. ID. NO. 44 C C C A A G G T C C G C A A G T G C C T G G C C A  
SEQ. ID. NO. 42 G G T G T G C T C C C C G C C G T G G A A C T G G

SEQ. ID. NO. 44 A C G G C T C C T G G A C A G A T A T G G A C A C  
SEQ. ID. NO. 42 C C A T C G A G C A G A T C C G C A A C G A G T C

SEQ. ID. NO. 44 A C C C A G C C G C T G T G T C C G A A T C T G C  
SEQ. ID. NO. 42 A C T C C T G C G C C C T T A C T T C C T C G A C

*FIG. 13a.*

SUBSTITUTE SHEET (RULE 26)

94/III

SEQ. ID. NO. 44 T C C A A G T C T T A T T T G A C C C T G G A A A  
SEQ. ID. NO. 42 C T G C G G C T C T A T G A C A C G G A G T G C G

SEQ. ID. NO. 44 A T G G G A A G G T T T T C C T G A C G G G T G G  
SEQ. ID. NO. 42 A C A A C G C A A A A G G G T T G A A A G C C T T

SEQ. ID. NO. 44 G G A C C T C C C A G C T C T G G A C G G A G C C  
SEQ. ID. NO. 42 C T A C G A T G C A A T A A A A T A C G G G G C C G

SEQ. ID. NO. 44 C G G G T G G A T T T C C G G T G T G A C C C C G  
SEQ. ID. NO. 42 A A C C A C T T G A T G G T G T T T G G A G G C G

SEQ. ID. NO. 44 A C T T C C A T C T G G T G G G C A G C T C C C G  
SEQ. ID. NO. 42 T C T G T C C A T C C G T C A C A T C C A T C A T

SEQ. ID. NO. 44 G A G C A T C T G T A G T C A G G G C C A G T G G  
SEQ. ID. NO. 42 T G C A G A G T C C C T C C A A G G C T G G A A T

SEQ. ID. NO. 44 A G C A C C C C C A A G C C C C A C T G C C A G G  
SEQ. ID. NO. 42 C T G G T G C A G C T T T T C T T T T G C T G C A A

SEQ. ID. NO. 44 T G A A T C G A A C G C C C A C A C T C A G A A C G  
SEQ. ID. NO. 42 C C A C G C C T G T T C T A G C C G A T A A G A A

SEQ. ID. NO. 44 G C G C G C A G T G T A C A T C G G G G C A C T G  
SEQ. ID. NO. 42 A A A A T A C C C T T A T T T C T T T C G G A C C

SEQ. ID. NO. 44 T T T C C C A T G A G C G G G G G C T G G C C A G  
SEQ. ID. NO. 42 G T C C C A T C A G A C A A T G C G G T G A A T C

SEQ. ID. NO. 44 G G G G C C A G G C C T G C C A G C C C G C G G T  
SEQ. ID. NO. 42 C A G C C A T T C T G A A G T T G C T C A A G C A

SEQ. ID. NO. 44 G G A G A T G G C G C T G G A G G A C G T G A A T  
SEQ. ID. NO. 42 C T A C C A G T G G A A G C G C G T G G G C A C G

SEQ. ID. NO. 44 A G C C G C A G G G A C A T C C T G C C G G A C T  
SEQ. ID. NO. 42 C T G A C G C A A G A C G T T C A G A G G T T C T

*FIG. 13b.*

SUBSTITUTE SHEET (RULE 26)

95/III

SEQ. ID. NO. 44 A T G A G C T C A A G C T C A T C C A C C A C G A  
SEQ. ID. NO. 42 C T G A G G T G C G G A A T G A C C T G A C T G G

SEQ. ID. NO. 44 C A G C A A G T G T G A T C C A G G C C A A G C C  
SEQ. ID. NO. 42 A G T T C T G T A T G G C G A G G A C A T T G A G

SEQ. ID. NO. 44 A C C A A G T A C C T A T A T G A G C T G C T C T  
SEQ. ID. NO. 42 A T T T C A G A C A C C G A G A G C T T C T C C A

SEQ. ID. NO. 44 A C A A C G A C C C T A T C A A G A T C A T C C T  
SEQ. ID. NO. 42 A C G A T C C C T G T A C C A G T G T C A A A A A

SEQ. ID. NO. 44 T A T G C C T G G C T G C A G C T C T G T C T C C  
SEQ. ID. NO. 42 G C T G A A G G G G A A T G A T G T G C G G A T C

SEQ. ID. NO. 44 A C G C T G G T G G C T G A G G C T G C T A G G A  
SEQ. ID. NO. 42 A T C C T T G G C C A G T T T G A C C A G A A T A

SEQ. ID. NO. 44 T G T G G A A C C T C A T T G T G C T T T C C T A  
SEQ. ID. NO. 42 T G G C A G C A A A A G T G T T C T G T T G T G C

SEQ. ID. NO. 44 T G G C T C C A G C T C A C C A G C C C T G T C A  
SEQ. ID. NO. 42 A T A C G A G G A G A A C A T G T A T G G T A G T

SEQ. ID. NO. 44 A A C C G G C A G C G T T T C C C C A C T T T C T  
SEQ. ID. NO. 42 A A A T A T C A G T G G A T C A T T C C G G G C T

SEQ. ID. NO. 44 T C C G A A C G C A C C C A T C A G C C A C A C T  
SEQ. ID. NO. 42 G G T A C G A G C C T T C T T G G T G G G A G C A

SEQ. ID. NO. 44 C C A C A A C C C T A C C C G C G T G A A A C T C  
SEQ. ID. NO. 42 G G T G C A C A C G G A A G C C A A C T C A T C C

SEQ. ID. NO. 44 T T T G A A A A G T G G G G C T G G A A G A A G A  
SEQ. ID. NO. 42 C G C T G C C T C C G G A A G A A T C T G C T T G

SEQ. ID. NO. 44 T T G C T A C C A T C C A G C A G A C C A C T G A  
SEQ. ID. NO. 42 C T G C C A T G G A G G G C T A C A T T G G C G T

FIG. 13c.  
SUBSTITUTE SHEET (RULE 26)

96/III

SEQ. ID. NO. 44 G G T C T T C A C T T C G A C T C T G G A C G A C  
SEQ. ID. NO. 42 G G A T T T C G A G C C C C T G A G C T C C A A G

SEQ. ID. NO. 44 C T G G A G G A A C G A G T G A A G G A G G C T G  
SEQ. ID. NO. 42 C A G A T C A A G A C C A T C T C A G G A A A G A

SEQ. ID. NO. 44 G A A T T G A G A T T A C T T T C C G C C A G A G  
SEQ. ID. NO. 42 C T C C A C A G C A G T A T G A G A G A G A G T A

SEQ. ID. NO. 44 T T T C T T C T C A G A T C C A G C T G T G C C C  
SEQ. ID. NO. 42 C A A C A A C A A G C G G T C A G G C G T G G G G

SEQ. ID. NO. 44 G T C A A A A A C C T G A A G C G C C A G G A T G  
SEQ. ID. NO. 42 C C C A G C A A G T T C C A C G G G T A C G C C T

SEQ. ID. NO. 44 C C C G A A T C A T C G T G G G A C T T T T T C T A  
SEQ. ID. NO. 42 A C G A T G G C A T C T G G G T C A T C G C C A A

SEQ. ID. NO. 44 T G A G A C T G A A G C C C G G A A A G T T T T T  
SEQ. ID. NO. 42 G A C A C T G C A G A G G G C C A T G G A G A C A

SEQ. ID. NO. 44 T G T G A G G T G T A C A A G G A G C G T C T C T  
SEQ. ID. NO. 42 C T G C A T G C C A G C A G C C G G C A C C A G C

SEQ. ID. NO. 44 T T G G G A A G A A G T A C G T C T G G T T C C T  
SEQ. ID. NO. 42 G G A T C C A G G A C T T C A A C T A C A C G G A

SEQ. ID. NO. 44 C A T T G G G T G G T A T G C T G A C A A T T G G  
SEQ. ID. NO. 42 C C A C A C G C T G G G C A G G A T C A T C C T C

SEQ. ID. NO. 44 T T C A A G A T C T A C G A C C C T T C T A T C A  
SEQ. ID. NO. 42 A A T G C C A T G A A C G A G A C C A A C T T C T

SEQ. ID. NO. 44 A C T G C A C A G T G G A T G A G A T G A C T G A  
SEQ. ID. NO. 42 T C G G G G T C A C G G G T C A A G T T G T A T T

SEQ. ID. NO. 44 G G C G G T G G A G G G C C A C A T C A C A A C T  
SEQ. ID. NO. 42 C C G G A A T G G G G A G A G A A T G G G G A C C

*FIG. 13d.*

SUBSTITUTE SHEET (RULE 26)



97/III

SEQ. ID. NO. 44 G A G A T T G T C A T G C T G A A T C C T G C C A  
SEQ. ID. NO. 42 A T T A A A T T T A C T C A A T T T C A A G A C A

SEQ. ID. NO. 44 A T A C C C G C A G C A T T T C C A A C A T G A C  
SEQ. ID. NO. 42 G C A G G G A G G T G A A G G T G G G A G A G T A

SEQ. ID. NO. 44 A T C C C A G G A A T T T G T G G A G A A A C T A  
SEQ. ID. NO. 42 C A A C G C T G T G G C C G A C A C A C T G G A G

SEQ. ID. NO. 44 A C C A A G C G A C T G A A A A G A C A C C C T G  
SEQ. ID. NO. 42 A T C A T C A A T G A C A C C A T C A G G T T C C

SEQ. ID. NO. 44 A G G A G A C A G G A G G C T T C C A G G A G G C  
SEQ. ID. NO. 42 A A G G A T C C G A A C C A C C A A A A G A C A A

SEQ. ID. NO. 44 A C C G C T G G C C T A T G A T G C C A T C T G G  
SEQ. ID. NO. 42 G A C C A T C A T C C T G G A G C A G C T G C G G

SEQ. ID. NO. 44 G C C T T G G C A C T G G C C C T G A A C A A G A  
SEQ. ID. NO. 42 A A G A T C T C C C T A C C T C T C T A C A G C A

SEQ. ID. NO. 44 C A T C T G G A G G A G G C G G C C G T T C T G G  
SEQ. ID. NO. 42 T C C T C T C T G C C C T C A C C A T C C T C G G

SEQ. ID. NO. 44 T G T G C G C C T G G A G G A C T T C A A C T A C  
SEQ. ID. NO. 42 G A T G A T C A T G G C C A G T G C T T T T C T C

SEQ. ID. NO. 44 A A C A A C C A G A C C A T T A C C G A C C A A A  
SEQ. ID. NO. 42 T T C T T C A A C A T C A A G A A C C G G A A T C

SEQ. ID. NO. 44 T C T A C C G G G C A A T G A A C T C T T C G T C  
SEQ. ID. NO. 42 A G A A G C T C A T A A A G A T G T C G A G T C C

SEQ. ID. NO. 44 C T T T G A G G G T G T C T C T G G C C A T G T G  
SEQ. ID. NO. 42 A T A C A T G A A C A A C C T T A T C A T C C T T

SEQ. ID. NO. 44 G T G T T T G A T G C C A G C G G C T C T C G G A  
SEQ. ID. NO. 42 G G A G G G A T G C T C T C C T A T G C T T C C A

*FIG. 13e.*  
SUBSTITUTE SHEET (RULE 26)

98/III

SEQ. ID. NO. 44 T G G C A T G G A C G C T T A T C G A G C A G C T  
SEQ. ID. NO. 42 T A T T T C T C T T T G G C C T T G A T G G A T C

SEQ. ID. NO. 44 T C A G G G T G G C A G C T A C A A G A A G A T T  
SEQ. ID. NO. 42 C T T T G T C T C T G A A A A G A C C T T T G A A

SEQ. ID. NO. 44 G G C T A C T A T G A C A G C A C C A A G G A T G  
SEQ. ID. NO. 42 A C A C T T T G C A C C G T C A G G A C C T G G A

SEQ. ID. NO. 44 A T C T T T C C T G G T C C A A A A C A G A T A A  
SEQ. ID. NO. 42 T T C T C A C C G T G G G C T A C A C G A C C G C

SEQ. ID. NO. 44 A T G G A T T G G A G G G T C C C C C C A G C T  
SEQ. ID. NO. 42 T T T T G G G G C C A T G T T T G C A A A G A C C

SEQ. ID. NO. 44 G A C C A G A C C C T G G T C A T C A A G A C A T  
SEQ. ID. NO. 42 T G G A G A G T C C A C G C C A T C T T C A A A A

SEQ. ID. NO. 44 T C C G C T T C C T G T C A C A G A A A C T C T T  
SEQ. ID. NO. 42 A T G T G A A A A T G A A G A A G A A G A T C A T

SEQ. ID. NO. 44 T A T C T C C G T C T C A G T T C T C T C C A G C  
SEQ. ID. NO. 42 C A A G G A C C A G A A A C T G C T T G T G A T C

SEQ. ID. NO. 44 C T G G G C A T T G T C C T A G C T G T T G T C T  
SEQ. ID. NO. 42 G T G G G G G G C A T G C T G C T G A T C G A C C

SEQ. ID. NO. 44 G T C T G T C C T T T A A C A T C T A C A A C T C  
SEQ. ID. NO. 42 T G T G T A T C C T G A T C T G C T G G C A G G C

SEQ. ID. NO. 44 A C A T G T C C G T T A T A T C C A G A A C T C A  
SEQ. ID. NO. 42 T G T G G A C C C C C T G C G A A G G A C A G T G

SEQ. ID. NO. 44 C A G C C C A A C C T G A A C A A C C T G A C T G  
SEQ. ID. NO. 42 G A G A A G T A C A G C A T G G A G C C G G A C C

SEQ. ID. NO. 44 C T G T G G G C T G C T C A C T G G C T T T A G C  
SEQ. ID. NO. 42 C A G C A G G A C G G G A T A T C T C C A T C C G

*FIG. 13f.*  
SUBSTITUTE SHEET (RULE 26)

99/III

SEQ. ID. NO. 44 T G C T G T C T T C C C C C T G G G G C T C G A T  
SEQ. ID. NO. 42 C C C T C T C C T G G A G C A C T G T G A G A A C

SEQ. ID. NO. 44 G G T T A C C A C A T T G G G A G G A A C C A G T  
SEQ. ID. NO. 42 A C C C A T A T G A C C A T C T G G C T T G G C A

SEQ. ID. NO. 44 T T C C T T T C G T C T G C C A G G C C C G C C T  
SEQ. ID. NO. 42 T C G T C T A T G C C T A C A A G G G A C T T C T

SEQ. ID. NO. 44 C T G G C T C C T G G G C C T G G G C T T T A G T  
SEQ. ID. NO. 42 C A T G T T G T T C G G T T G T T T C T T A G C T

SEQ. ID. NO. 44 C T G G G C T A C G G T T C C A T G T T C A C C A  
SEQ. ID. NO. 42 T G G G A G A C C C G C A A C G T C A G C A T C C

SEQ. ID. NO. 44 A G A T T T G G T G G G T C C A C A C G G T C T T  
SEQ. ID. NO. 42 C C G C A C T C A A C G A C A G C A A G T A C A T

SEQ. ID. NO. 44 C A C A A A G A A G G A A G A A A A G A A G G A G  
SEQ. ID. NO. 42 C G G G A T G A G T G T C T A C A A C G T G G G G

SEQ. ID. NO. 44 T G G A G G A A G A C T C T G G A A C C C T G G A  
SEQ. ID. NO. 42 A T C A T G T G C A T C A T C G G G G C C G C T G

SEQ. ID. NO. 44 A G C T G T A T G C C A C A G T G G G C C T G C T  
SEQ. ID. NO. 42 T C T C C T T C C T G A C C C G G G A C C A G C C

SEQ. ID. NO. 44 G G T G G G C A T G G A T G T C C T C A C T C T C  
SEQ. ID. NO. 42 C A A T G T G C A G T T C T G C A T C G T G G C T

SEQ. ID. NO. 44 G C C A T C T G G C A G A T C G T G G A C C C T C  
SEQ. ID. NO. 42 C T G G T C A T C A T C T T C T G C A G C A C C A

SEQ. ID. NO. 44 T G C A C C G G A C C A T T G A G A C A T T T T G C  
SEQ. ID. NO. 42 T C A C C C T C T G C C T G G T A T T C G T G C C

SEQ. ID. NO. 44 C A A G G A G G A A C C T A A G G A A G A T A T T  
SEQ. ID. NO. 42 G A A G C T C A T C A C C C T G A G A A C A A A C

*FIG. 13g.*

SUBSTITUTE SHEET (RULE 26)

100/111

SEQ. ID. NO. 44 G A C G T C T C T A T T C T G C C C C A G C T G G  
SEQ. ID. NO. 42 C C A G A T G C A G C A A C G C A G A A C A G G C

SEQ. ID. NO. 44 A G C A T T G C A G C T C C A G G A A G A T G A A  
SEQ. ID. NO. 42 G A T T C C A G T T C A C T C A G A A T C A G A A

SEQ. ID. NO. 44 T A C A T G G C T T G G C A T T T T C T A T G G T  
SEQ. ID. NO. 42 G A A A G A A G A T T C T A A A A C G T C C A C C

SEQ. ID. NO. 44 T A C A A G G G G C T G C T G C T G C T G C T G G  
SEQ. ID. NO. 42 T C G G T C A C C A G T G T G A A C C A A G C C A

SEQ. ID. NO. 44 G A A T C T T C C T T G C T T A T G A G A C C A A  
SEQ. ID. NO. 42 G C A C A T C C C G C C T G G A G G G C C T A C A

SEQ. ID. NO. 44 G A G T G T G T C C A C T G A G A A G A T C A A T  
SEQ. ID. NO. 42 G T C A G A A A A C C A T C G C C T G C G A A T G

SEQ. ID. NO. 44 G A T C A C C G G G C T G T G G G C A T G G C T A  
SEQ. ID. NO. 42 A A G A T C A C A G A G C T G G A T A A A G A C T

SEQ. ID. NO. 44 T C T A C A A T G T G G C A G T C C T G T G C C T  
SEQ. ID. NO. 42 T G G A A G A G G T C A C C A T G C A G C T G C A

SEQ. ID. NO. 44 C A T C A C T G C T C C T G T C A C C A T G A T T  
SEQ. ID. NO. 42 G G A C A C A C C A G A A A A G A C C A C C T A C

SEQ. ID. NO. 44 C T G T C C A G C C A G C A G G A T G C A G C C T  
SEQ. ID. NO. 42 A T T A A A C A G A A C C A C T A C C A A G A G C

SEQ. ID. NO. 44 T T G C C T T T G C C T C T C T T G C C A T A G T  
SEQ. ID. NO. 42 T C A A T G A C A T C C T C A A C C T G G G A A A

SEQ. ID. NO. 44 T T T C T C C T C C T A T A T C A C T C T T G T T  
SEQ. ID. NO. 42 C T T C A C T G A G A G C A C A G A T G G A G G A

SEQ. ID. NO. 44 G T G C T C T T T G T G C C C A A G A T G C G C A  
SEQ. ID. NO. 42 A A G G C C A T T T T A A A A A A T C A C C T C G

*FIG. 13h.*

SUBSTITUTE SHEET (RULE 26)

101/III

SEQ. ID. NO. 44 G G C T G A T C A C C C G A G G G G A A T G G C A  
SEQ. ID. NO. 42 A T C A A A A T C C C C A G C T A C A G T G G A A

SEQ. ID. NO. 44 G T C G G A G G C G C A G G A C A C C A T G A A G  
SEQ. ID. NO. 42 C A C A A C A G A G C C C T C T C G A A C A T G C

SEQ. ID. NO. 44 A C A G G G T C A T C G A C C A A C A A C A A C G  
SEQ. ID. NO. 42 A A A G A T C C T A T A G A A G A T A T A A A C T

SEQ. ID. NO. 44 A G G A G G A G A A G T C C C G G C T G T T G G A  
SEQ. ID. NO. 42 C T C C A G A A C A C A T C C A G C G T C G G C T

SEQ. ID. NO. 44 G A A G G A G A A C C G T G A A C T G G A A A A G  
SEQ. ID. NO. 42 G T C C C T C C A G C T C C C C A T C C T C C A C

SEQ. ID. NO. 44 A T C A T T G C T G A G A A A G A G G A G C G T G  
SEQ. ID. NO. 42 C A C G C C T A C C T C C C A T C C A T C G G A G

SEQ. ID. NO. 44 T C T C T G A A C T G C G C C A T C A A C T C C A  
SEQ. ID. NO. 42 G C G T G G A C G C C A G C T G T G T C A G C C C

SEQ. ID. NO. 44 G T C T C G G C A G C A G C T C C G C T C C C G G  
SEQ. ID. NO. 42 C T G C G T C A G C C C C A C C G C C A G C C C C

SEQ. ID. NO. 44 C G C C A C C C A C C G A C A C C C C C A G A A C  
SEQ. ID. NO. 42 C G C C A C A G A C A T G T G C C A C C C T C C T

SEQ. ID. NO. 44 C C T C T G G G G G C C T G C C C A G G G G A C C  
SEQ. ID. NO. 42 T C C G A G T C A T G G T C T C G G G C C T G G C

SEQ. ID. NO. 44 C C C T G A G C C C C C C G A C C G G C T T A G C  
SEQ. ID. NO. 42 G G C C G C C A T G A C T C T G G A G T C C A T C

SEQ. ID. NO. 44 T G T G A T G G G A G T C G A G T G C A T T T G C  
SEQ. ID. NO. 42 A T G G C G T G C T G C C T G A G C G A G G A G G

SEQ. ID. NO. 44 T T T A T A A G G C G G C C G C C A T G A C T C T  
SEQ. ID. NO. 42 C C A A G G A A G C C C G G C G G A T C A A C G A

*FIG. 13i.*

SUBSTITUTE SHEET (RULE 26)

102/III

SEQ. ID. NO. 44 G G A G T C C A T C A T G G C G T G C T G C C T G  
SEQ. ID. NO. 42 C G A G A T C G A G C G G C A G C T C C G C A G G

SEQ. ID. NO. 44 A G C G A G G A G G C C A A G G A A G C C C G G C  
SEQ. ID. NO. 42 G A C A A G C G G G A C G C C C G C C G G G A G C

SEQ. ID. NO. 44 G G A T C A A C G A C G A G A T C G A G C G G C A  
SEQ. ID. NO. 42 T C A A G C T G C T G C T G C T C G G G A C A G G

SEQ. ID. NO. 44 G C T C C G C A G G G A C A A G C G G G A C G C C  
SEQ. ID. NO. 42 A G A G A G T G G C A A G A G T A C G T T T A T C

SEQ. ID. NO. 44 C G C C G G G A G C T C A A G C T G C T G C T G C  
SEQ. ID. NO. 42 A A G C A G A T G A G A A T C A T C C A T G G G T

SEQ. ID. NO. 44 T C G G G A C A G G A G A G A G T G G C A A G A G  
SEQ. ID. NO. 42 C A G G A T A C T C T G A T G A A G A T A A A A G

SEQ. ID. NO. 44 T A C G T T T A T C A A G C A G A T G A G A A T C  
SEQ. ID. NO. 42 G G G C T T C A C C A A G C T G G T G T A T C A G

SEQ. ID. NO. 44 A T C C A T G G G T C A G G A T A C T C T G A T G  
SEQ. ID. NO. 42 A A C A T C T T C A C G G C C A T G C A G G C C A

SEQ. ID. NO. 44 A A G A T A A A A G G G G C T T C A C C A A G C T  
SEQ. ID. NO. 42 T G A T C A G A G C C A T G G A C A C A C T C A A

SEQ. ID. NO. 44 G G T G T A T C A G A A C A T C T T C A C G G C C  
SEQ. ID. NO. 42 G A T C C C A T A C A A G T A T G A G C A C A A T

SEQ. ID. NO. 44 A T G C A G G C C A T G A T C A G A G C C A T G G  
SEQ. ID. NO. 42 A A G G C T C A T G C A C A A T T A G T T C G A G

SEQ. ID. NO. 44 A C A C A C T C A A G A T C C C A T A C A A G T A  
SEQ. ID. NO. 42 A A G T T G A T G T G G A G A A G G T G T C T G C

SEQ. ID. NO. 44 T G A G C A C A A T A A G G C T C A T G C A C A A  
SEQ. ID. NO. 42 T T T T G A G A A T C C A T A T G T A G A T G C A

*FIG. 13j.*

SUBSTITUTE SHEET (RULE 26)

103/III

SEQ. ID. NO. 44 T T A G T T C G A G A A G T T G A T G T G G A G A  
SEQ. ID. NO. 42 A T A A A G A G T T T A T G G A A T G A T C C T G

SEQ. ID. NO. 44 A G G T G T C T G C T T T T G A G A A T C C A T A  
SEQ. ID. NO. 42 G A A T C C A G G A A T G C T A T G A T A G A C G

SEQ. ID. NO. 44 T G T A G A T G C A A T A A A G A G T T T A T G G  
SEQ. ID. NO. 42 A C G A G A A T A T C A A T T A T C T G A C T C T

SEQ. ID. NO. 44 A A T G A T C C T G G A A T C C A G G A A T G C T  
SEQ. ID. NO. 42 A C C A A A T A C T A T C T T A A T G A C T T G G

SEQ. ID. NO. 44 A T G A T A G A C G A C G A G A A T A T C A A T T  
SEQ. ID. NO. 42 A C C G C G T A G C T G A C C C T G C C T A C C T

SEQ. ID. NO. 44 A T C T G A C T C T A C C A A A T A C T A T C T T  
SEQ. ID. NO. 42 G C C T A C G C A A C A A G A T G T G C T T A G A

SEQ. ID. NO. 44 A A T G A C T T G G A C C G C G T A G C T G A C C  
SEQ. ID. NO. 42 G T T C G A G T C C C C A C C A C A G G G A T C A

SEQ. ID. NO. 44 C T G C C T A C C T G C C T A C G C A A C A A G A  
SEQ. ID. NO. 42 T C G A A T A C C C C T T T G A C T T A C A A A G

SEQ. ID. NO. 44 T G T G C T T A G A G T T C G A G T C C C C A C C  
SEQ. ID. NO. 42 T G T C A T T T T T C A G A A T G G T C G A T G T A

SEQ. ID. NO. 44 A C A G G G A T C A T C G A A T A C C C C T T T G  
SEQ. ID. NO. 42 G G G G G C C A A A G G T C A G A G A G A A G A A

SEQ. ID. NO. 44 A C T T A C A A A G T G T C A T T T T T C A G A A T  
SEQ. ID. NO. 42 A A T G G A T A C A C T G C T T T T G A A A A T G T

SEQ. ID. NO. 44 G G T C G A T G T A G G G G G C C A A A G G T C A  
SEQ. ID. NO. 42 C A C C T C T A T C A T G T T T T C T A G T A G C G

SEQ. ID. NO. 44 G A G A G A A G A A A A T G G A T A C A C T G C T  
SEQ. ID. NO. 42 C T T A G T G A A T A T G A T C A A G T T C T G G

*FIG. 13k.*

SUBSTITUTE SHEET (RULE 26)

104/III

SEQ. ID. NO. 44 TTGAA AATGTCACCTCTATCATGTT  
SEQ. ID. NO. 42 TGGAGTTCAGACAATGAGAACCGAAT

SEQ. ID. NO. 44 TCTAGTAGCGCTTAGTGAAATATGAT  
SEQ. ID. NO. 42 GGAGGAAAGCAAGGCTCTCTTTAGA

SEQ. ID. NO. 44 CAAGTTCTCTGTGGAGTCAGACAATG  
SEQ. ID. NO. 42 ACAATTATCACATACCCCTGGTTCC

SEQ. ID. NO. 44 AGAACC GAATGGAGGAAAGCAAGGC  
SEQ. ID. NO. 42 AGAACTCCTCGGTTATTCTGTTCTT

SEQ. ID. NO. 44 TCTCTTTAGAACAAATTATCACATAC  
SEQ. ID. NO. 42 AAACAAGAAAGATCTTCTAGAGGAG

SEQ. ID. NO. 44 CCCTGGTTTCCAGAACTCCTCGGTTA  
SEQ. ID. NO. 42 AAAATCATGTATTCCCATCTAGTCG

SEQ. ID. NO. 44 TTCTGTTCTTAAACAAGAAAGATCT  
SEQ. ID. NO. 42 ACTACTTCCCAGAAATATGATGGACC

SEQ. ID. NO. 44 TCTAGAGGAGAAAAATCATGTATTCC  
SEQ. ID. NO. 42 CCAGAGAGATGCCCAGGCAGCCCCGA

SEQ. ID. NO. 44 CATCTAGTCGACTACTTCCCAGAAAT  
SEQ. ID. NO. 42 GAATTCAATTCTGAAGATGTTCTGTGG

SEQ. ID. NO. 44 ATGATGGACCC CAGAGAGATGCCCA  
SEQ. ID. NO. 42 ACCTGAACCC CAGACAGTGACAAAAT

SEQ. ID. NO. 44 GGCAGCCCGAGAAATTCATTCTGAAG  
SEQ. ID. NO. 42 TAACTACTCCC ACTTTCACGTGCGCC

SEQ. ID. NO. 44 ATGTTCTGTGGACCTGAACCCAGACA  
SEQ. ID. NO. 42 ACAGACACCCGAGAAATATCCGCTTTG

SEQ. ID. NO. 44 GTGACAAAATTATCTACTCCC ACTT  
SEQ. ID. NO. 42 TCTTTGCTGCCGTCAAAGGACACCAT

FIG. 13L

SUBSTITUTE SHEET (RULE 26)



105/III

SEQ. ID. NO. 44 C A C G T G C G C C A C A G A C A C C G A G A A T  
SEQ. ID. NO. 42 C C T C C A G T T G A A C C T G A A G G G C T G C

SEQ. ID. NO. 44 A T C C G C T T T G T C T T T G C T G C C G T C A  
SEQ. ID. NO. 42 G G T C T G T A C

SEQ. ID. NO. 44 A G G A C A C C A T C C T C C A G T T G A A C C T  
SEQ. ID. NO. 42

SEQ. ID. NO. 44 G A A G G G C T G C G G T C T G T A C  
SEQ. ID. NO. 42

*FIG. 13m.*

106/III

## ClustalW Formatted Alignments

SEQ. ID. NO. 45 M L L L L L L A P L F L R P P G A G G A Q T P N A  
SEQ. ID. NO. 43 M A S P R S S G Q P G P P P P P P P P A R L L L

SEQ. ID. NO. 45 T S E G C Q I I H P P W E G G I R Y R G L T R D Q  
SEQ. ID. NO. 43 L L L L P L L L P L A P G A W G W A R G A P R P P

SEQ. ID. NO. 45 V K A I N F L P V D Y E I E Y V C R G E R E V V G  
SEQ. ID. NO. 43 P S S P P L S I M G L M P L T K E V A K G S I G R

SEQ. ID. NO. 45 P K V R K C L A N G S W T D M D T P S R C V R I C  
SEQ. ID. NO. 43 G V L P A V E L A I E Q I R N E S L L R P Y F L D

SEQ. ID. NO. 45 S K S Y L T L E N G K V F L T G G D L P A L D G A  
SEQ. ID. NO. 43 L R L Y D T E C D N A K G L K A F Y D A I K Y G P

SEQ. ID. NO. 45 R V D F R C D P D F H L V G S S R S I C S Q G Q W  
SEQ. ID. NO. 43 N H L M V F G G V C P S V T S I I A E S L Q G W N

SEQ. ID. NO. 45 S T P K P H C Q V N R T P H S E R R A V Y I G A L  
SEQ. ID. NO. 43 L V Q L S F A A T T P V L A D K K K Y P Y F F R T

SEQ. ID. NO. 45 F P M S G G W P G G Q A C Q P A V E M A L E D V N  
SEQ. ID. NO. 43 V P S D N A V N P A I L K L L K H Y Q W K R V G T

SEQ. ID. NO. 45 S R R D I L P D Y E L K L I H H D S K C D P G Q A  
SEQ. ID. NO. 43 L T Q D V Q R F S E V R N D L T G V L Y G E D I E

SEQ. ID. NO. 45 T K Y L Y E L L Y N D P I K I I L M P G C S S V S  
SEQ. ID. NO. 43 I S D T E S F S N D P C T S V K K L K G N D V R I

SEQ. ID. NO. 45 T L V A E A A R M W N L I V L S Y G S S S P A L S  
SEQ. ID. NO. 43 I L G Q F D Q N M A A K V F C C A Y E E N M Y G S

SEQ. ID. NO. 45 N R Q R F P T F F R T H P S A T L H N P T R V K L  
SEQ. ID. NO. 43 K Y Q W I I P G W Y E P S W W E Q V H T E A N S S

FIG. 14a.

107/III

SEQ. ID. NO. 45 FEKVGWKKIATIQQTTEVFTSTLDD  
 SEQ. ID. NO. 43 RCLRKNNLLAAMEGYIGVDFEPLSSK

SEQ. ID. NO. 45 LEERVKEAGIEITFRQSFFSDPAVP  
 SEQ. ID. NO. 43 QIKTISGKTPQQYEREYNNKRSGVG

SEQ. ID. NO. 45 VKNLKRQDARIIVGLFYETEARKVVF  
 SEQ. ID. NO. 43 PSKFHGYAYDGIWVIAKTLQRAMET

SEQ. ID. NO. 45 CEVYKERLFGKKYVWFLIGWYADNW  
 SEQ. ID. NO. 43 LHASSRHQRIQDFNYTDHTLGRIL

SEQ. ID. NO. 45 FKIYDPSINCTVDEMTEAVEGHITT  
 SEQ. ID. NO. 43 NAMNETNFFFGVGTGQVVFRNGERMGT

SEQ. ID. NO. 45 EIVMLNPANTRSI SNMTS QEFVEKL  
 SEQ. ID. NO. 43 IKFTQFQDSREVKVGEYNAVADTLE

SEQ. ID. NO. 45 TKRLKRHPREETGG - FQEAPLAYDAI  
 SEQ. ID. NO. 43 IINDTIRFQGSEPPKDKTIILEQLR

SEQ. ID. NO. 45 WALALALNKTS GGGGRSGVRLDFN  
 SEQ. ID. NO. 43 KISLPLYSILSALTILGMIMASAFLL

SEQ. ID. NO. 45 YNNQTITDQIYRAMNSSSSFEGVSGH  
 SEQ. ID. NO. 43 FFNIKNRNQKLIKMS SPYMNNLIIL

SEQ. ID. NO. 45 VVFDASGSRMAWTLIEQLQGGSYKK  
 SEQ. ID. NO. 43 GGMLSYASIFLFGLDGSFVSEKTFE

SEQ. ID. NO. 45 IGYDSTKDDL SWSKTDKWIGGSPP  
 SEQ. ID. NO. 43 TLCTVRTWILTVGYTTAFGAMFAKT

SEQ. ID. NO. 45 ADQTLVIKTFRFLSQKLFISVSVLS  
 SEQ. ID. NO. 43 WRVHAIFKNVKMKKKIKDKQLLVI

SEQ. ID. NO. 45 SLGIVLAVVCLSFNIYN SHVRYIQN  
 SEQ. ID. NO. 43 VGGMLLIDLCLICWQAVDPLRRTV

FIG. 14b.

108/III

SEQ. ID. NO. 45 S Q P N L N N L T A V G C S L A L A A V F P L G L  
 SEQ. ID. NO. 43 E K Y S M E P D P A G R D I S I R P L L E H C E N

SEQ. ID. NO. 45 D G Y H I G R N Q F P F V C Q A R L W L L G L G F  
 SEQ. ID. NO. 43 T H M T I W L G I V Y A Y K G L L M L F G C F L A

SEQ. ID. NO. 45 S L G Y G S M F T K I W W V H T V F T K K E E K K  
 SEQ. ID. NO. 43 W E T R N V S I P A L N D S K Y I G M S V Y N V G

SEQ. ID. NO. 45 E W R K T L E P W K L Y A T V G L L V G M D V L T  
 SEQ. ID. NO. 43 I M C I I G A A V S F L T R D Q P N V Q F C I V A

SEQ. ID. NO. 45 L A I W Q I V D P L H R T I E T F A K E E P K E D  
 SEQ. ID. NO. 43 L V I I F C S T I T L C L V F V P K L I T L R T N

SEQ. ID. NO. 45 I D V S I L P Q L E H C S S R K M N T W L G I F Y  
 SEQ. ID. NO. 43 P D A A T Q N R R F Q F T Q N Q K K E D S K T S T

SEQ. ID. NO. 45 G Y K G L L L L L G I F L A Y E T K S V S T E K I  
 SEQ. ID. NO. 43 S V T S V N Q A S T S R L E G L Q S E N H R L R M

SEQ. ID. NO. 45 N D H R A V G M A I Y N V A V L C L I T A P V T M  
 SEQ. ID. NO. 43 K I T E L D K D L E E V T M Q L Q D T P E K T T Y

SEQ. ID. NO. 45 I L S S Q Q D A A F A F A S L A I V F S S Y I T L  
 SEQ. ID. NO. 43 I K Q N H Y Q E L N D I L N L G N F T E S T D G G

SEQ. ID. NO. 45 V V L F V P K M R R L I T R G E W Q S E A Q D T M  
 SEQ. ID. NO. 43 K A I L K N H L D Q N P Q L Q W N T T E P S R T C

SEQ. ID. NO. 45 K T G S S T N N N E E E K S R L L E K E N R E L E  
 SEQ. ID. NO. 43 K D P I E D I N S P E H I Q R R L S L Q L P I L H

SEQ. ID. NO. 45 K I I A E K E E R V S E L R H Q L Q S R Q Q L R S  
 SEQ. ID. NO. 43 H A Y L P S I G G V D A S C V S P C V S P T A S P

SEQ. ID. NO. 45 R R H P P T P P E P S G G L P R G P P E P P D R L  
 SEQ. ID. NO. 43 R H R H V P P S F R V M V S G L A A A M T L E S I

FIG. 14c.

SUBSTITUTE SHEET (RULE 26)

109/III

SEQ. ID. NO. 45 SCDGSRVHLLYKAAAMTLESIMACC  
 SEQ. ID. NO. 43 MACCLSEEAKEARRINDEIERQLRR

SEQ. ID. NO. 45 LSEEAKEARRINDEIERQLRRDKRD  
 SEQ. ID. NO. 43 DKRDARRELKLLLLLGTGESGKSTFI

SEQ. ID. NO. 45 ARRELKLLLLLGTGESGKSTFIKQMR  
 SEQ. ID. NO. 43 KQMRIIHGSGYSDDEDKRGFTKLVYQ

SEQ. ID. NO. 45 I IHGSGYSDDEDKRGFTKLVYQNI FT  
 SEQ. ID. NO. 43 NI FTAMQAMIRAMDTLKI PYKYEHN

SEQ. ID. NO. 45 AMQAMIRAMDTLKI PYKYEHNKAHA  
 SEQ. ID. NO. 43 KAHAQLVREVDVEKVS AFENPYVDA

SEQ. ID. NO. 45 QLVREVDVEKVS AFENPYVDAIKSL  
 SEQ. ID. NO. 43 IKSLWNDPGIQECYDRRREYQLSDS

SEQ. ID. NO. 45 WNDPGIQECYDRRREYQLSDSTKY Y  
 SEQ. ID. NO. 43 TKYYLNDLDRVADPAYLP TQQQDVLR

SEQ. ID. NO. 45 LNDLDRVADPAYLP TQQQDVLRVRVP  
 SEQ. ID. NO. 43 VRVP TTGIIEY PFDLQSVIFRMVDV

SEQ. ID. NO. 45 TTGIIEY PFDLQSVIFRMVDVGGQR  
 SEQ. ID. NO. 43 GGQRSERRKWIHCFENVTSIMFLVA

SEQ. ID. NO. 45 SERRKWIHCFENVTSIMFLV A LSEY  
 SEQ. ID. NO. 43 LSEYDQVLVESDNENRMEESKALFR

SEQ. ID. NO. 45 DQVLVESDNENRMEESKALFR TIIT  
 SEQ. ID. NO. 43 TIITYPWFQNSSVILFLNKKDLLEE

SEQ. ID. NO. 45 YPWFQNSSVILFLNKKDLLEEKIMY  
 SEQ. ID. NO. 43 KIMYSHLVDFPEYDGPQRDAQAAR

SEQ. ID. NO. 45 SHLVDFPEYDGPQRDAQAAREFIL  
 SEQ. ID. NO. 43 EFILKMFVDLNPDS DKINYSHF TCA

*FIG. 14d.*

SUBSTITUTE SHEET (RULE 26)

110/111

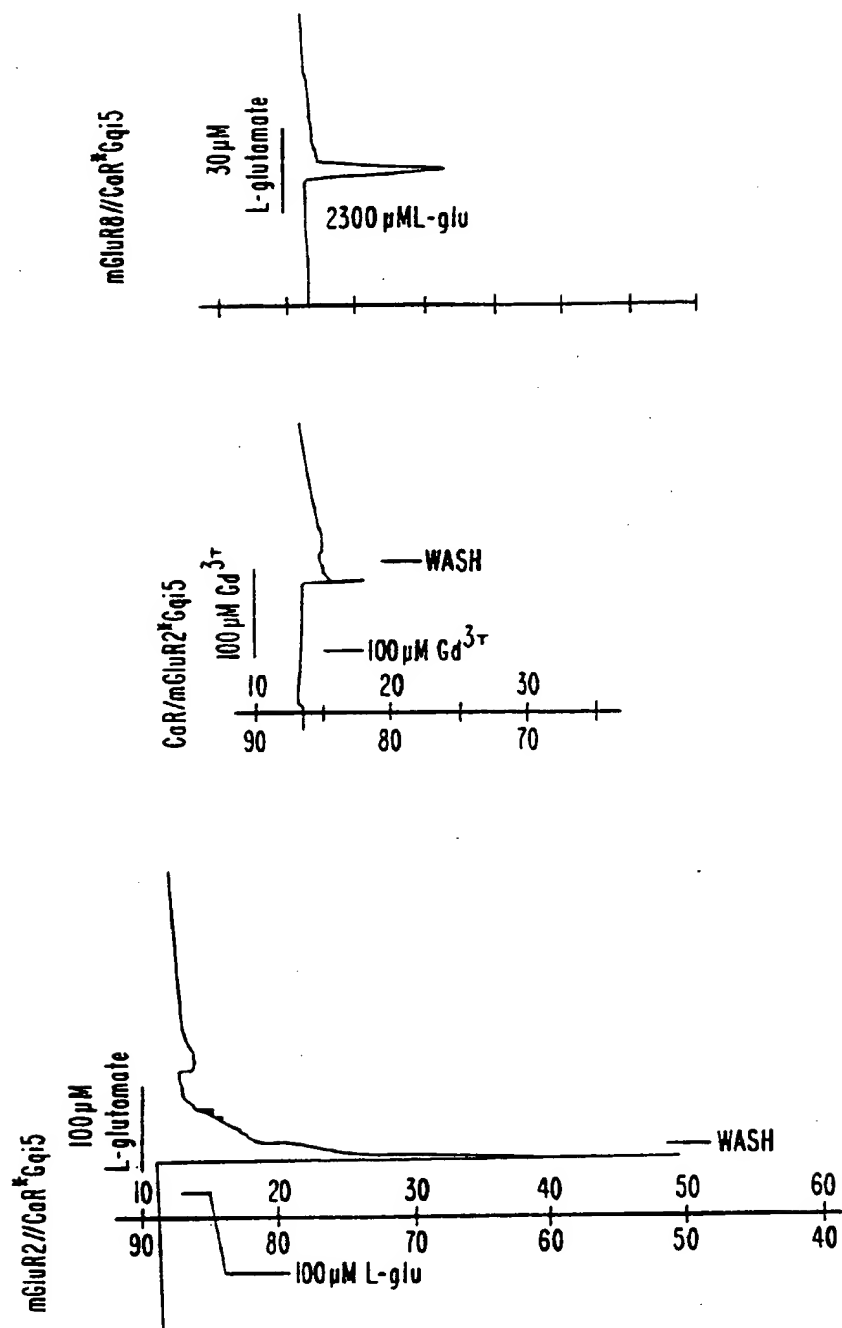
SEQ. ID. NO. 45 K M F V D L N P D S D K I I Y S H F T C A T D T E  
SEQ. ID. NO. 43 T D T E N I R F V F A A V K D T I L Q L N L K G C

SEQ. ID. NO. 45 N I R F V F A A V K D T I L Q L N L K G C G L Y  
SEQ. ID. NO. 43 G L Y

*FIG. 14e.*

III/III

FIG. 15.



SUBSTITUTE SHEET (RULE 26)

## SEQUENCE LISTING

<110> NPS PHARMACEUTICALS, INC.

<120> G-PROTEIN FUSION RECEPTORS AND CHIMERIC  
GABA<sub>B</sub> RECEPTORS

<130> 241/086-PCT

<140> TO BE ASSIGNED

<141> HEREWITH

<150> US 60/080,671

<151> 1998-04-03

<160> 47

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 612

<212> PRT

<213> Human

<400> 1

```
Met Ala Phe Tyr Ser Cys Cys Trp Val Leu Leu Ala Leu Thr Trp His
 1               5               10               15

Thr Ser Ala Tyr Gly Pro Asp Gln Arg Ala Gln Lys Lys Gly Asp Ile
 20               25               30

Ile Leu Gly Gly Leu Phe Pro Ile His Phe Gly Val Ala Ala Lys Asp
 35               40               45

Gln Asp Leu Lys Ser Arg Pro Glu Ser Val Glu Cys Ile Arg Tyr Asn
 50               55               60

Phe Arg Gly Phe Arg Trp Leu Gln Ala Met Ile Phe Ala Ile Glu Glu
 65               70               75               80

Ile Asn Ser Ser Pro Ala Leu Leu Pro Asn Leu Thr Leu Gly Tyr Arg
 85               90               95

Ile Phe Asp Thr Cys Asn Thr Val Ser Lys Ala Leu Glu Ala Thr Leu
 100              105              110
```



Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe  
 115 120 125  
 Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala  
 130 135 140  
 Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe  
 145 150 155 160  
 Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Arg Leu Leu Ser Asn  
 165 170 175  
 Lys Asn Gln Phe Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His  
 180 185 190  
 Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp  
 195 200 205  
 Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu  
 210 215 220  
 Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser  
 225 230 235 240  
 Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val  
 245 250 255  
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser  
 260 265 270  
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile  
 275 280 285  
 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu  
 290 295 300  
 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe  
 305 310 315 320  
 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys  
 325 330 335  
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp  
 340 345 350  
 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu  
 355 360 365  
 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe  
 370 375 380  
 Ser Asn Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn  
 385 390 395 400

3

Ile Ser Ser Val Glu Thr Pro Tyr Ile Asp Tyr Thr His Leu Arg Ile  
 405 410 415  
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln  
 420 425 430  
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser  
 435 440 445  
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu  
 450 455 460  
 Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp  
 465 470 475 480  
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu  
 485 490 495  
 Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn  
 500 505 510  
 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile  
 515 520 525  
 Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg  
 530 535 540  
 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr  
 545 550 555 560  
 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu  
 565 570 575  
 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn  
 580 585 590  
 Glu Asn His Thr Ser Cys Ile Ala Lys Glu Ile Glu Phe Leu Ser Trp  
 595 600 605  
 Thr Glu Pro Phe  
 610

<210> 2  
 <211> 590  
 <212> PRT  
 <213> Human

<400> 2

Met Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly  
 1 5 10 15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile  
 20 25 30  
 Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg  
 35 40 45  
 Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu  
 50 55 60  
 Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys  
 65 70 75 80  
 Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys  
 85 90 95  
 Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val  
 100 105 110  
 Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp  
 115 120 125  
 Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile  
 130 135 140  
 Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn  
 145 150 155 160  
 Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe  
 165 170 175  
 Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val  
 180 185 190  
 Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp  
 195 200 205  
 Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln  
 210 215 220  
 Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile  
 225 230 235 240  
 Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala  
 245 250 255  
 Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro  
 260 265 270  
 Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro  
 275 280 285  
 Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp  
 290 295 300

Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr  
 305 310 315 320  
 Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu  
 325 330 335  
 Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys  
 340 345 350  
 Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu  
 355 360 365  
 Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe  
 370 375 380  
 Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp  
 385 390 395 400  
 Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr  
 405 410 415  
 Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro  
 420 425 430  
 Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu  
 435 440 445  
 Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe  
 450 455 460  
 Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala  
 465 470 475 480  
 Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu  
 485 490 495  
 Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala  
 500 505 510  
 Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp  
 515 520 525  
 Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly  
 530 535 540  
 Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu  
 545 550 555 560  
 Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp  
 565 570 575  
 Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys  
 580 585 590

<210> 3  
 <211> 473  
 <212> PRT  
 <213> Human

<400> 3

```

Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
 1           5           10           15
Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
 20           25           30
Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
 35           40           45
Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
 50           55           60
Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
 65           70           75           80
Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
 85           90           95
Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
 100          105          110
Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
 115          120          125
Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
 130          135          140
Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
 145          150          155          160
Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
 165          170          175
Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
 180          185          190
Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
 195          200          205
Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
 210          215          220
Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
 225          230          235          240
Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
 245          250          255

```

7

Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val  
 260 265 270  
 Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp  
 275 280 285  
 Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly  
 290 295 300  
 His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser  
 305 310 315 320  
 Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg  
 325 330 335  
 Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu  
 340 345 350  
 Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser  
 355 360 365  
 Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn  
 370 375 380  
 Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser  
 385 390 395 400  
 Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg  
 405 410 415  
 Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys  
 420 425 430  
 Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr  
 435 440 445  
 Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile  
 450 455 460  
 Lys Thr Phe Arg Phe Leu Ser Gln Lys  
 465 470

<210> 4  
 <211> 480  
 <212> PRT  
 <213> Human

<400> 4

Met Ala Ser Pro Arg Ser Ser Gly Gln Pro Gly Pro Xaa Pro Pro Pro  
 1 5 10 15

Pro Pro Pro Pro Ala Arg Leu Leu Leu Leu Leu Leu Pro Leu Leu  
 20 25 30  
 Leu Pro Leu Ala Pro Gly Ala Trp Gly Trp Ala Arg Gly Ala Pro Arg  
 35 40 45  
 Pro Pro Pro Ser Ser Pro Pro Leu Ser Ile Met Gly Leu Met Pro Leu  
 50 55 60  
 Thr Lys Glu Val Ala Lys Gly Ser Ile Gly Arg Gly Val Leu Pro Ala  
 65 70 75 80  
 Val Glu Leu Ala Ile Glu Gln Ile Arg Asn Glu Ser Leu Leu Arg Pro  
 85 90 95  
 Tyr Phe Leu Asp Leu Arg Leu Tyr Asp Thr Glu Cys Asp Asn Ala Lys  
 100 105 110  
 Gly Leu Lys Ala Phe Tyr Asp Ala Ile Lys Tyr Gly Pro Asn His Leu  
 115 120 125  
 Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile Ala Glu  
 130 135 140  
 Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala Thr Thr  
 145 150 155 160  
 Pro Val Leu Ala Asp Lys Lys Lys Tyr Pro Tyr Phe Phe Arg Thr Val  
 165 170 175  
 Pro Ser Asp Asn Ala Val Asn Pro Ala Ile Leu Lys Leu Leu Lys His  
 180 185 190  
 Tyr Gln Trp Lys Arg Val Gly Thr Leu Thr Gln Asp Val Gln Arg Phe  
 195 200 205  
 Ser Glu Val Arg Asn Asp Leu Thr Gly Val Leu Tyr Gly Glu Asp Ile  
 210 215 220  
 Glu Ile Ser Asp Thr Glu Ser Phe Ser Asn Asp Pro Cys Thr Ser Val  
 225 230 235 240  
 Lys Lys Leu Lys Gly Asn Asp Val Arg Ile Ile Leu Gly Gln Phe Asp  
 245 250 255  
 Gln Asn Met Ala Ala Lys Val Phe Cys Cys Ala Tyr Glu Glu Asn Met  
 260 265 270  
 Tyr Gly Ser Lys Tyr Gln Trp Ile Ile Pro Gly Trp Tyr Glu Pro Ser  
 275 280 285  
 Trp Trp Glu Gln Val His Thr Glu Ala Asn Ser Ser Arg Cys Leu Arg  
 290 295 300  
 Lys Asn Leu Leu Ala Ala Met Glu Gly Tyr Ile Gly Val Asp Phe Glu  
 305 310 315 320

Pro	Leu	Ser	Ser	Lys	Gln	Ile	Lys	Thr	Ile	Ser	Gly	Lys	Thr	Pro	Gln	
				325						330					335	
Gln	Tyr	Glu	Arg	Glu	Tyr	Asn	Asn	Lys	Arg	Ser	Gly	Val	Gly	Pro	Ser	
			340					345					350			
Lys	Phe	His	Gly	Tyr	Ala	Tyr	Asp	Gly	Ile	Trp	Val	Ile	Ala	Lys	Thr	
		355					360					365				
Leu	Gln	Arg	Ala	Met	Glu	Thr	Leu	His	Ala	Ser	Ser	Arg	His	Gln	Arg	
	370					375					380					
Ile	Gln	Asp	Phe	Asn	Tyr	Thr	Asp	His	Thr	Leu	Gly	Arg	Ile	Ile	Leu	
385					390					395					400	
Asn	Ala	Met	Asn	Glu	Thr	Asn	Phe	Phe	Gly	Val	Thr	Gly	Gln	Val	Val	
				405					410					415		
Phe	Arg	Asn	Gly	Glu	Arg	Met	Gly	Thr	Ile	Lys	Phe	Thr	Gln	Phe	Gln	
			420					425					430			
Asp	Ser	Arg	Glu	Val	Lys	Val	Gly	Glu	Tyr	Asn	Ala	Val	Ala	Asp	Thr	
			435				440					445				
Leu	Glu	Ile	Ile	Asn	Asp	Thr	Ile	Arg	Phe	Gln	Gly	Ser	Glu	Pro	Pro	
	450					455					460					
Lys	Asp	Lys	Thr	Ile	Ile	Leu	Glu	Gln	Leu	Arg	Lys	Ile	Ser	Leu	Pro	
465					470					475					480	

<210>	5
<211>	583
<212>	PRT
<213>	Human

<400> 5

Met	Val	Cys	Glu	Gly	Lys	Arg	Ser	Ala	Ser	Cys	Pro	Cys	Phe	Phe	Leu
1				5					10					15	
Leu	Thr	Ala	Lys	Phe	Tyr	Trp	Ile	Leu	Thr	Met	Met	Gln	Arg	Thr	His
			20					25					30		
Ser	Gln	Glu	Tyr	Ala	His	Ser	Ile	Arg	Val	Asp	Gly	Asp	Ile	Ile	Leu
		35					40					45			
Gly	Gly	Leu	Phe	Pro	Val	His	Ala	Lys	Gly	Glu	Arg	Gly	Val	Pro	Cys
	50					55					60				
Gly	Glu	Leu	Lys	Lys	Glu	Lys	Gly	Ile	His	Arg	Leu	Glu	Ala	Met	Leu
65					70					75					80



10

Tyr Ala Ile Asp Gln Ile Asn Lys Asp Pro Asp Leu Leu Ser Asn Ile  
 85 90 95  
 Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala  
 100 105 110  
 Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala  
 115 120 125  
 Ser Asp Val Lys Cys Ala Asn Gly Asp Pro Pro Ile Phe Thr Lys Pro  
 130 135 140  
 Asp Lys Ile Ser Gly Val Ile Gly Ala Ala Ala Ser Ser Val Ser Ile  
 145 150 155 160  
 Met Val Ala Asn Ile Leu Arg Leu Phe Lys Ile Pro Gln Ile Ser Tyr  
 165 170 175  
 Ala Ser Thr Ala Pro Glu Leu Ser Asp Asn Thr Arg Tyr Asp Phe Phe  
 180 185 190  
 Ser Arg Val Val Pro Pro Asp Ser Tyr Gln Ala Gln Ala Met Val Asp  
 195 200 205  
 Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu  
 210 215 220  
 Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg  
 225 230 235 240  
 Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu  
 245 250 255  
 Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr  
 260 265 270  
 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg  
 275 280 285  
 Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu  
 290 295 300  
 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln  
 305 310 315 320  
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala  
 325 330 335  
 Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn  
 340 345 350  
 Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly  
 355 360 365

11

Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys  
 370 375 380  
 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly  
 385 390 395 400  
 Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu  
 405 410 415  
 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro  
 420 425 430  
 Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala  
 435 440 445  
 Val Asn Phe Asn Gly Ser Ala Gly Thr Pro Val Thr Phe Asn Glu Asn  
 450 455 460  
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn  
 465 470 475 480  
 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His  
 485 490 495  
 Leu Lys Val Glu Asp Met Gln Trp Ala His Arg Glu His Thr His Pro  
 500 505 510  
 Ala Ser Val Cys Ser Leu Pro Cys Lys Pro Gly Glu Arg Lys Lys Thr  
 515 520 525  
 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr  
 530 535 540  
 Asn Tyr Gln Val Asp Glu Leu Ser Cys Glu Leu Cys Pro Leu Asp Gln  
 545 550 555 560  
 Arg Pro Asn Met Asn Arg Thr Gly Cys Gln Leu Ile Pro Ile Ile Lys  
 565 570 575  
 Leu Glu Trp His Ser Pro Trp  
 580

&lt;210&gt; 6

&lt;211&gt; 250

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 6

Gly Ile Ala Leu Thr Leu Phe Ala Val Leu Gly Ile Phe Leu Thr Ala  
 1 5 10 15

12

Phe Val Leu Gly Val Phe Ile Lys Phe Arg Asn Thr Pro Ile Val Lys  
 20 25 30  
 Ala Thr Asn Arg Glu Leu Ser Tyr Leu Leu Leu Phe Ser Leu Leu Cys  
 35 40 45  
 Cys Phe Ser Ser Ser Leu Phe Phe Ile Gly Glu Pro Gln Asp Trp Thr  
 50 55 60  
 Cys Arg Leu Arg Gln Pro Ala Phe Gly Ile Ser Phe Val Leu Cys Ile  
 65 70 75 80  
 Ser Cys Ile Leu Val Lys Thr Asn Arg Val Leu Leu Val Phe Glu Ala  
 85 90 95  
 Lys Ile Pro Thr Ser Phe His Arg Lys Trp Trp Gly Leu Asn Leu Gln  
 100 105 110  
 Phe Leu Leu Val Phe Leu Cys Thr Phe Met Gln Ile Val Ile Cys Val  
 115 120 125  
 Ile Trp Leu Tyr Thr Ala Pro Pro Ser Ser Tyr Arg Asn Gln Glu Leu  
 130 135 140  
 Glu Asp Glu Ile Ile Phe Ile Thr Cys His Glu Gly Ser Leu Met Ala  
 145 150 155 160  
 Leu Gly Phe Leu Ile Gly Tyr Thr Cys Leu Leu Ala Ala Ile Cys Phe  
 165 170 175  
 Phe Phe Ala Phe Lys Ser Arg Lys Leu Pro Glu Asn Phe Asn Glu Ala  
 180 185 190  
 Lys Phe Ile Thr Phe Ser Met Leu Ile Phe Phe Ile Val Trp Ile Ser  
 195 200 205  
 Phe Ile Pro Ala Tyr Ala Ser Thr Tyr Gly Lys Phe Val Ser Ala Val  
 210 215 220  
 Glu Val Ile Ala Ile Leu Ala Ala Ser Phe Gly Leu Leu Ala Cys Ile  
 225 230 235 240  
 Phe Phe Asn Lys Ile Tyr Ile Ile Leu Phe  
 245 250

<210> 7  
 <211> 267  
 <212> PRT  
 <213> Human

&lt;400&gt; 7

Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala  
 1 5 10 15  
 Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile  
 20 25 30  
 Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser  
 35 40 45  
 Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile  
 50 55 60  
 Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu  
 65 70 75 80  
 Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp  
 85 90 95  
 Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg  
 100 105 110  
 Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val  
 115 120 125  
 Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu  
 130 135 140  
 His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile  
 145 150 155 160  
 Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met  
 165 170 175  
 Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu  
 180 185 190  
 Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys  
 195 200 205  
 Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val  
 210 215 220  
 Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln  
 225 230 235 240  
 Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr  
 245 250 255  
 Ile Thr Leu Val Val Leu Phe Val Pro Lys Met  
 260 265

<210> 8  
 <211> 267  
 <212> PRT  
 <213> Human

<400> 8

```

Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
 1              5              10              15

Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
      20              25              30

Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
      35              40              45

Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
 50              55              60

Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
 65              70              75              80

Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
      85              90              95

Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
      100              105              110

Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
      115              120              125

Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
      130              135              140

His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
      145              150              155              160

Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
      165              170              175

Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
      180              185              190

Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
      195              200              205

Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
      210              215              220

Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
      225              230              235              240

```

15

Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr  
                                   245                                  250                                  255

Ile Thr Leu Val Val Leu Phe Val Pro Lys Met  
                                   260                                  265

<210> 9  
 <211> 264  
 <212> PRT  
 <213> Human

<400> 9

Leu Tyr Ser Ile Leu Ser Ala Leu Thr Ile Leu Gly Met Ile Met Ala  
   1                                  5                                  10                                  15

Ser Ala Phe Leu Phe Phe Asn Ile Lys Asn Arg Asn Gln Lys Leu Ile  
                                   20                                  25                                  30

Lys Met Ser Ser Pro Tyr Met Asn Asn Leu Ile Ile Leu Gly Gly Met  
                                   35                                  40                                  45

Leu Ser Tyr Ala Ser Ile Phe Leu Phe Gly Leu Asp Gly Ser Phe Val  
   50                                  55                                  60

Ser Glu Lys Thr Phe Glu Thr Leu Cys Thr Val Arg Thr Trp Ile Leu  
   65                                  70                                  75                                  80

Thr Val Gly Tyr Thr Thr Ala Phe Gly Ala Met Phe Ala Lys Thr Trp  
                                   85                                  90                                  95

Arg Val His Ala Ile Phe Lys Asn Val Lys Met Lys Lys Lys Ile Ile  
                                   100                                  105                                  110

Lys Asp Gln Lys Leu Leu Val Ile Val Gly Gly Met Leu Leu Ile Asp  
                                   115                                  120                                  125

Leu Cys Ile Leu Ile Cys Trp Gln Ala Val Asp Pro Leu Arg Arg Thr  
   130                                  135                                  140

Val Glu Lys Tyr Ser Met Glu Pro Asp Pro Ala Gly Arg Asp Ile Ser  
   145                                  150                                  155                                  160

Ile Arg Pro Leu Leu Glu His Cys Glu Asn Thr His Met Thr Ile Trp  
                                   165                                  170                                  175

Leu Gly Ile Val Tyr Ala Tyr Lys Gly Leu Leu Met Leu Phe Gly Cys  
                                   180                                  185                                  190

Phe Leu Ala Trp Glu Thr Arg Asn Val Ser Ile Pro Ala Leu Asn Asp  
                                   195                                  200                                  205

16

Ser Lys Tyr Ile Gly Met Ser Val Tyr Asn Val Gly Ile Met Cys Ile  
 210 215 220

Ile Gly Ala Ala Val Ser Phe Leu Thr Arg Asp Gln Pro Asn Val Gln  
 225 230 235 240

Phe Cys Ile Val Ala Leu Val Ile Ile Phe Cys Ser Thr Ile Thr Leu  
 245 250 255

Cys Leu Val Phe Val Pro Lys Leu  
 260

<210> 10  
 <211> 260  
 <212> PRT  
 <213> Human

<400> 10

Ala Val Val Pro Val Phe Val Ala Ile Leu Gly Ile Ile Ala Thr Thr  
 1 5 10 15

Phe Val Ile Val Thr Phe Val Arg Tyr Asn Asp Thr Pro Ile Val Arg  
 20 25 30

Ala Ser Gly Arg Glu Leu Ser Tyr Val Leu Leu Thr Gly Ile Phe Leu  
 35 40 45

Cys Tyr Ser Ile Thr Phe Leu Met Ile Ala Ala Pro Asp Thr Ile Ile  
 50 55 60

Cys Ser Phe Arg Arg Val Phe Leu Gly Leu Gly Met Cys Phe Ser Tyr  
 65 70 75 80

Ala Ala Leu Leu Thr Lys Thr Asn Arg Ile His Arg Ile Phe Glu Gln  
 85 90 95

Gly Lys Lys Ser Val Thr Ala Pro Lys Phe Ile Ser Pro Ala Ser Gln  
 100 105 110

Leu Val Ile Thr Phe Ser Leu Ile Ser Val Gln Leu Leu Gly Val Phe  
 115 120 125

Val Trp Phe Val Val Asp Pro Pro His Ile Ile Ile Asp Tyr Gly Glu  
 130 135 140

Gln Arg Thr Leu Asp Pro Glu Lys Ala Arg Gly Val Leu Lys Cys Asp  
 145 150 155 160

Ile Ser Asp Leu Ser Leu Ile Cys Ser Leu Gly Tyr Ser Ile Leu Leu  
 165 170 175

17

Met Val Thr Cys Thr Val Tyr Ala Ile Lys Thr Arg Gly Val Pro Glu  
 180 185 190

Thr Phe Asn Glu Ala Lys Pro Ile Gly Phe Thr Met Tyr Thr Thr Cys  
 195 200 205

Ile Ile Trp Leu Ala Phe Ile Pro Ile Phe Phe Gly Thr Ala Gln Ser  
 210 215 220

Ala Glu Lys Met Tyr Ile Gln Thr Thr Thr Leu Thr Val Ser Met Ser  
 225 230 235 240

Leu Ser Ala Ser Val Ser Leu Gly Met Leu Tyr Met Pro Lys Val Tyr  
 245 250 255

Ile Ile Ile Phe  
 260

<210> 11  
 <211> 216  
 <212> PRT  
 <213> Human

<400> 11

Lys Pro Ser Arg Asn Thr Ile Glu Glu Val Arg Cys Ser Thr Ala Ala  
 1 5 10 15

His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg Ser Asn Val  
 20 25 30

Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro  
 35 40 45

Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln  
 50 55 60

Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr Gln Gln Glu  
 65 70 75 80

Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln  
 85 90 95

Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr  
 100 105 110

Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met Ala His Gly  
 115 120 125

Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr  
 130 135 140



18

Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp  
 145 150 155 160  
 Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly  
 165 170 175  
 Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu  
 180 185 190  
 Val Val Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr  
 195 200 205  
 Val Thr Glu Asn Val Val Asn Ser  
 210 215

<210> 12  
 <211> 104  
 <212> PRT  
 <213> Human

<400> 12

Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr  
 1 5 10 15  
 Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg  
 20 25 30  
 Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys  
 35 40 45  
 Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln  
 50 55 60  
 Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly  
 65 70 75 80  
 Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly  
 85 90 95  
 Ser Arg Val His Leu Leu Tyr Lys  
 100

<210> 13  
 <211> 104  
 <212> PRT  
 <213> Human

19

&lt;400&gt; 13

Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr  
 1 5 10 15  
 Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg  
 20 25 30  
 Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys  
 35 40 45  
 Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln  
 50 55 60  
 Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly  
 65 70 75 80  
 Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly  
 85 90 95  
 Ser Arg Val His Leu Leu Tyr Lys  
 100

<210> 14  
 <211> 197  
 <212> PRT  
 <213> Human

&lt;400&gt; 14

Ile Thr Leu Arg Thr Asn Pro Asp Ala Ala Thr Gln Asn Arg Arg Phe  
 1 5 10 15  
 Gln Phe Thr Gln Asn Gln Lys Lys Glu Asp Ser Lys Thr Ser Thr Ser  
 20 25 30  
 Val Thr Ser Val Asn Gln Ala Ser Thr Ser Arg Leu Glu Gly Leu Gln  
 35 40 45  
 Ser Glu Asn His Arg Leu Arg Met Lys Ile Thr Glu Leu Asp Lys Asp  
 50 55 60  
 Leu Glu Glu Val Thr Met Gln Leu Gln Asp Thr Pro Glu Lys Thr Thr  
 65 70 75 80  
 Tyr Ile Lys Gln Asn His Tyr Gln Glu Leu Asn Asp Ile Leu Asn Leu  
 85 90 95  
 Gly Asn Phe Thr Glu Ser Thr Asp Gly Gly Lys Ala Ile Leu Lys Asn  
 100 105 110

[illegible]

<210>	15
<211>	65
<212>	PRT
<213>	Human

<400> 15

[illegible]

<210> 16  
<211> 374  
<212> PRT  
<213> Human

<400> 16

Met Ala Arg Ser Leu Thr Trp Gly Cys Cys Pro Trp Cys Leu Thr Glu  
1 5 10 15

21

Glu Glu Lys Thr Ala Ala Arg Ile Asp Gln Glu Ile Asn Arg Ile Leu  
 20 25 30  
 Leu Glu Gln Lys Lys Gln Glu Arg Glu Glu Leu Lys Leu Leu Leu Leu  
 35 40 45  
 Gly Pro Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile  
 50 55 60  
 Ile His Gly Val Gly Tyr Ser Glu Glu Asp Arg Arg Ala Phe Arg Leu  
 65 70 75 80  
 Leu Ile Tyr Gln Asn Ile Phe Val Ser Met Gln Ala Met Ile Asp Ala  
 85 90 95  
 Met Asp Arg Leu Gln Ile Pro Phe Ser Arg Pro Asp Ser Lys Gln His  
 100 105 110  
 Ala Ser Leu Val Met Thr Gln Asp Pro Tyr Lys Val Ser Thr Phe Glu  
 115 120 125  
 Lys Pro Tyr Ala Val Ala Met Gln Tyr Leu Trp Arg Asp Ala Gly Ile  
 130 135 140  
 Arg Ala Cys Tyr Glu Arg Arg Arg Glu Phe His Leu Leu Asp Ser Ala  
 145 150 155 160  
 Val Tyr Tyr Leu Ser His Leu Glu Arg Ile Ser Glu Asp Ser Tyr Ile  
 165 170 175  
 Pro Thr Ala Gln Asp Val Leu Arg Ser Arg Met Pro Thr Thr Gly Ile  
 180 185 190  
 Asn Glu Tyr Cys Phe Ser Val Lys Lys Thr Lys Leu Arg Ile Val Asp  
 195 200 205  
 Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu  
 210 215 220  
 Asn Val Ile Ala Leu Ile Tyr Leu Ala Ser Leu Ser Glu Tyr Asp Gln  
 225 230 235 240  
 Cys Leu Glu Glu Asn Asp Gln Glu Asn Arg Met Glu Glu Ser Leu Ala  
 245 250 255  
 Leu Phe Ser Thr Ile Leu Glu Leu Pro Trp Phe Lys Ser Thr Ser Val  
 260 265 270  
 Ile Leu Phe Leu Asn Lys Thr Asp Ile Leu Glu Asp Lys Ile His Thr  
 275 280 285  
 Ser His Leu Ala Thr Tyr Phe Pro Ser Phe Gln Gly Pro Arg Arg Asp  
 290 295 300

22

Ala Glu Ala Ala Lys Ser Phe Ile Leu Asp Met Tyr Ala Arg Val Tyr  
 305 310 315 320

Ala Ser Cys Ala Glu Pro Gln Asp Gly Gly Arg Lys Gly Ser Arg Ala  
 325 330 335

Arg Arg Phe Phe Ala His Phe Thr Cys Ala Thr Asp Thr Gln Ser Val  
 340 345 350

Arg Ser Val Phe Lys Asp Val Arg Asp Ser Val Leu Ala Arg Tyr Leu  
 355 360 365

Asp Glu Ile Asn Leu Leu  
 370

<210> 17  
 <211> 374  
 <212> PRT  
 <213> Human

<400> 17

Met Ala Arg Ser Leu Thr Trp Arg Cys Cys Pro Trp Cys Leu Thr Glu  
 1 5 10 15

Asp Glu Lys Ala Ala Ala Arg Val Asp Gln Glu Ile Asn Arg Ile Leu  
 20 25 30

Leu Glu Gln Lys Lys Gln Asp Arg Gly Glu Leu Lys Leu Leu Leu Leu  
 35 40 45

Gly Pro Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile  
 50 55 60

Ile His Gly Ala Gly Tyr Ser Glu Glu Glu Arg Lys Gly Phe Arg Pro  
 65 70 75 80

Leu Val Tyr Gln Asn Ile Phe Val Ser Met Arg Ala Met Ile Glu Ala  
 85 90 95

Met Glu Arg Leu Gln Ile Pro Phe Ser Arg Pro Glu Ser Lys His His  
 100 105 110

Ala Ser Leu Val Met Ser Gln Asp Pro Tyr Lys Val Thr Thr Phe Glu  
 115 120 125

Lys Arg Tyr Ala Ala Ala Met Gln Trp Leu Trp Arg Asp Ala Gly Ile  
 130 135 140

Arg Ala Cys Tyr Glu Arg Arg Arg Glu Phe His Leu Leu Asp Ser Ala  
 145 150 155 160

23

Val Tyr Tyr Leu Ser His Leu Glu Arg Ile Thr Glu Glu Gly Tyr Val  
 165 170 175  
 Pro Thr Ala Gln Asp Val Leu Arg Ser Arg Met Pro Thr Thr Gly Ile  
 180 185 190  
 Asn Glu Tyr Cys Phe Ser Val Gln Lys Thr Asn Leu Arg Ile Val Asp  
 195 200 205  
 Val Gly Gly Gln Lys Ser Glu Arg Lys Lys Trp Ile His Cys Phe Glu  
 210 215 220  
 Asn Val Ile Ala Leu Ile Tyr Leu Ala Ser Leu Ser Glu Tyr Asp Gln  
 225 230 235 240  
 Cys Leu Glu Glu Asn Asn Gln Glu Asn Arg Met Lys Glu Ser Leu Ala  
 245 250 255  
 Leu Phe Gly Thr Ile Leu Glu Leu Pro Trp Phe Lys Ser Thr Ser Val  
 260 265 270  
 Ile Leu Phe Leu Asn Lys Thr Asp Ile Leu Glu Glu Lys Ile Pro Thr  
 275 280 285  
 Ser His Leu Ala Thr Tyr Phe Pro Ser Phe Gln Gly Pro Lys Gln Asp  
 290 295 300  
 Ala Glu Ala Ala Lys Arg Phe Ile Leu Asp Met Tyr Thr Arg Met Tyr  
 305 310 315 320  
 Thr Gly Cys Val Asp Gly Pro Glu Gly Ser Lys Lys Gly Ala Arg Ser  
 325 330 335  
 Arg Arg Leu Phe Ser His Tyr Thr Cys Ala Thr Asp Thr Gln Asn Ile  
 340 345 350  
 Arg Lys Val Phe Lys Asp Val Arg Asp Ser Val Leu Ala Arg Tyr Leu  
 355 360 365  
 Asp Glu Ile Asn Leu Leu  
 370

&lt;210&gt; 18

&lt;211&gt; 3234

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 18

atggcatttt atagctgctg ctgggtcctc ttggcactca cctggcacac ctctgcctac 60  
 gggccagacc agcgagccca aaagaagggg gacattatcc ttgggggggt ctttcctatt 120  
 cattttggag tagcagctaa agatcaagat ctcaaataca ggccggagtc tgtggaatgt 180

atcagggtata	atttccgtgg	gtttcgctgg	ttacaggcta	tgatatttgc	catagaggag	240
ataaacagca	gcccagccct	tcttcccaac	ttgacgctgg	gatacaggat	atttgaact	300
tgcaacaccg	tttctaaggc	cttggaagcc	accctgagtt	ttgttgctca	aaacaaaatt	360
gattctttga	accttgatga	gttctgcaac	tgctcagagc	acattccctc	tacgattgct	420
gtggtgggag	caactggctc	aggcgtctcc	acggcagtg	caaactctgt	ggggctcttc	480
tacattcccc	aggtcagtta	tgcttcctcc	agcagactcc	tcagcaacaa	gaatcaattc	540
aagtctttcc	tccgaaccat	ccccaatgat	gagcaccagg	ccactgccat	ggcagacatc	600
atcgagtatt	tccgctggaa	ctgggtgggc	acaattgcag	ctgatgacga	ctatgggcgg	660
ccggggattg	agaaattccg	agaggaagct	gaggaaagg	atatctgcat	cgacttcagt	720
gaactcatct	cccagtactc	tgatgaggaa	gagatccagc	atgtggtaga	ggtgattcaa	780
aattccacgg	ccaaagtcat	cgtgggtttc	tccagtggcc	cagatcttga	gcccctcatc	840
aaggagattg	tccggcgcaa	tatcacgggc	aagatctggc	tggccagcga	ggcctgggcc	900
agctcctccc	tgatcgccat	gcctcagtac	ttccacgtgg	ttggcggcac	cattggattc	960
gctctgaagg	ctgggcagat	cccaggcttc	cgggaattcc	tgaagaaggt	ccatcccagg	1020
aagtctgtcc	acaatggttt	tgccaaggag	ttttgggaag	aaacatttaa	ctgccacctc	1080
caagaagggtg	caaaaggacc	tttacctgtg	gacacctttc	tgagagggtca	cgaagaaagt	1140
ggcgacagg	ttagcaacag	ctcgacagcc	ttccgacccc	tctgtacagg	ggatgagaac	1200
atcagcagtg	tcgagacccc	ttacatagat	tacacgcatt	tacggatata	ctacaatgtg	1260
tacttagcag	tctactccat	tgcccacgcc	ttgcaagata	tatatactcg	cttacctggg	1320
agagggctct	tcaccaatgg	ctcctgtgca	gacatcaaga	aagttgaggc	gtggcaggctc	1380
ctgaagcacc	tacggcatct	aaactttaca	aacaatatgg	gggagcagg	gacctttgat	1440
gagtggtgg	acctggtggg	gaactattcc	atcatcaact	ggcacctctc	cccagaggat	1500
ggctccatcg	tgtttaagga	agtcgggtat	tacaacgtct	atgccaagaa	gggagaaaaga	1560
ctcttcataca	acgaggagaa	aatcctgtgg	agtgggttct	ccagggaggt	gaccttctcc	1620
aactgcagcc	gagactgcct	ggcagggacc	aggaaaggga	tcattgagg	ggagcccacc	1680
tgctgctttg	agtgtgtgga	gtgtcctgat	ggggagtata	gtgatgagac	agatgccagt	1740
gcctgtaaca	agtgcccaga	tgacttctgg	tccaatgaga	accacacctc	ctgcattgcc	1800
aaggagatcg	agtttctgtc	gtggacggag	ccctttggga	tcgactcac	cctctttgcc	1860
gtgctgggca	ttttcttgac	agcctttgtg	ctgggtgtgt	ttatcaagtt	ccgcaacaca	1920
cccattgtca	aggccaccaa	ccgagagctc	tctacctccc	tcctcttctc	ctcgtctg	1980
tgcttctcca	gctccctgtt	cttcacggg	gagccccagg	actggacgtg	ccgcctgcgc	2040
cagccggcct	ttggcatcag	cttcgtgtc	tgcatctcat	gcacctggt	gaaaaccaac	2100
cgtgtcctcc	tggtgtttga	ggccaagatc	cccaccagct	tccaccgcaa	gtggtggggg	2160
ctcaacctgc	agttcctgct	ggttttctc	tgacacctca	tgagattgt	catctgtgtg	2220
atctggctct	acaccgcgcc	cccccaagc	taccgcaacc	aggagctgga	ggatgagatc	2280
atcttcatca	cgtgccacga	gggtccctc	atggccctgg	gcttctgtat	cggctacacc	2340
tgctgctgg	ctgccatctg	cttcttcttt	gccttcaagt	cccggaagct	gccggagaa	2400
ttcaatgaag	ccaagttcat	caccttcagc	atgctcatct	tcttcatcgt	ctggatctcc	2460
ttcattccag	cctatgccag	cacctatggc	aagtttgtct	ctgccgtaga	ggtgattgcc	2520
atcctggcag	ccagctttgg	cttgctggcg	tgcatcttct	tcaacaagat	ctacatcatt	2580
ctcttcaagc	catcccga	caccatcgag	gaggtgcgtt	gcagcaccgc	agctcacgct	2640
ttcaagggtg	ctgcccgggc	cacgctgcgc	cgcagcaacg	tctcccga	gcggctccagc	2700
agccttgag	gctccacggg	atccaccccc	tcctctcca	tcagcagcaa	gagcaacagc	2760
gaagacccat	tcccacagcc	cgagaggcag	aagcagcagc	agccgctggc	cctaaccacg	2820
caagagcagc	agcagcagcc	cctgaccctc	ccacagcagc	aacgatctca	gcagcagccc	2880
agatgcaagc	agaaggtcat	ctttggcagc	ggcacggtca	ccttctcact	gagctttgat	2940
gagcctcaga	agaacgccat	ggcccacggg	aattctacgc	accagaactc	cctggaggcc	3000
cagaaaagca	gcgatacgct	gacccgacac	cagccattac	tcccgtgca	gtgcgggaa	3060
acggacttag	atctgaccgt	ccaggaaaca	ggtctgcaag	gacctgtggg	tggagaccag	3120
cggccagagg	tggaggaccc	tgaagagttg	tccccagcac	ttgtagtgtc	cagttcacag	3180
agctttgtca	tcagtgtgtg	aggcagcact	gttacagaaa	acgtagtga	ttca	3234

<210> 19  
 <211> 3464  
 <212> DNA  
 <213> Human

<400> 19

atgttgctgc	tgtgtgtact	ggcgccactc	tctctccgcc	ccccggggcg	ggcgggggcg	60
cagaccccc	acgccacctc	agaagggtgc	cagatcatac	acccgccctg	ggaagggggc	120
atcaggtacc	ggggcctgac	tcgggaccag	gtgaaggcta	tcaacttcct	gccagtggac	180
tatgagattg	agtatgtgtg	ccggggggag	cgcgagggtg	tggggcccaa	ggtccgcaag	240
tgcctggcca	acggctcctg	gacagatatg	gacacaccca	gccgtgtgt	ccgaatctgc	300
tccaagtctt	atttgaccct	ggaaaatggg	aaggttttcc	tgacgggtgg	ggacctccca	360
gctctggacg	gagcccggtg	ggattttccg	tgtgaccccg	acttccatct	ggtgggcage	420
tcccgagaca	tctgtagtca	gggccagtgg	agcaccacca	agccccaactg	ccaggtgaat	480
cgaacgccac	actcagaacg	gcgcgcagtg	tacatcgggg	caactgtttcc	catgagcggg	540
ggctggccag	ggggccaggc	ctgccagccc	gcgggtggaga	tggcgctgga	ggacgtgaat	600
agccgcaggg	acatcctgcc	ggactatgag	ctcaagctca	tccaccacga	cagcaagtgt	660
gatccaggcc	aagccaccaa	gtacctatat	gagctgtctt	acaacgaccc	tatcaagatc	720
atccttatgc	ctggctgcag	ctctgtctcc	acgctgggtg	ctgaggctgc	taggatgtgg	780
aacctcattg	tgctttcccta	tggctccagc	tcaccagccc	tgtcaaaccg	gcagcgtttc	840
cccactttct	tccgaacgca	cccatcagcc	acaactccaca	accctacccg	cgtgaaactc	900
tttgaaaagt	ggggctggaa	gaagattgct	accatccagc	agaccactga	ggtcttccact	960
tcgactctgg	acgacctgga	ggaacgagtg	aaggaggctg	gaattgagat	tactttccgc	1020
cagagtttct	tctcagatcc	agctgtgccc	gtcaaaaacc	tgaagcgcca	ggatgcccga	1080
atcatcgtgg	gacttttcta	tgagactgaa	gcccggaaa	ttttttgtga	ggtgtacaag	1140
gagcgtctct	ttgggaagaa	gtacgtctgg	tctctcattg	ggtgggtatg	tgacaattgg	1200
ttcaagatct	acgaccttc	tatcaactgc	acagtggatg	agatgactga	ggcggtggag	1260
ggccacatca	caactgagat	tgtcatgctg	aatcctgcc	atacccgag	catttccaac	1320
atgacatccc	aggaatttgt	ggagaaaacta	accaagcgac	tgaaaagaca	ccctgaggag	1380
acaggaggct	tccaggaggc	accgctggcc	tatgatgcc	tctgggcctt	ggcactggcc	1440
ctgaacaaga	catctggagg	aggcgggcgt	tctggtgtgc	gcctggagga	cttcaactac	1500
aacaaccaga	ccattaccga	ccaaatctac	cgggcaatga	actcttcgtc	ctttgagggt	1560
gtctctggcc	atgtggtgtt	tgatgccagc	ggctctcgga	tggcatggac	gcttatcgag	1620
cagcttcagg	gtggcagcta	caagaagatt	ggctactatg	acagcaccaa	ggatgatctt	1680
tcttggtcca	aaacagataa	atggattgga	gggtccccc	cagctgacca	gacctgggtc	1740
atcaagacat	tccgcttcct	gtcacagaaa	ctctttatct	ccgtctcagt	tctctccagc	1800
ctgggcattg	tcttagctgt	tgtctgtctg	tctttaaca	tctacaactc	acatgtccgt	1860
tatatccaga	actcacagcc	caacctgaac	aacctgactg	ctgtgggctg	ctcactggct	1920
ttagctgctg	tcttccccct	ggggctcgat	ggttaccaca	ttgggaggaa	ccagtttccct	1980
ttcgtctgcc	aggcccgcc	ctggctcctg	ggcctgggct	ttagtctggg	ctacggttcc	2040
atgttcacca	agatttggtg	ggtccacacg	gtcttcacaa	agaaggaa	aaagaaggag	2100
tggagggaaga	ctctggaacc	ctggaagctg	tatgccacag	tgggcctgct	ggtgggcag	2160
gatgtcctca	ctctcgccat	ctggcagatc	gtggaccctc	tgcaccggac	cattgagaca	2220
tttgccaagg	aggaacctaa	ggaagatatt	gacgtctcta	ttctgcccc	gctggagcat	2280
tgcagctcca	ggaagatgaa	tacatggctt	ggcattttct	atggttacia	ggggctgctg	2340
ctgctgctgg	gaatcttcc	tgttatgag	accaagagtg	tgtccactga	gaagatcaat	2400
gatcaccggg	ctgtgggcat	ggctatctac	aatgtggcag	tctgtgcct	catcactgct	2460
cctgtcacca	tgattctgtc	cagccagcag	gatgcagcct	ttgcctttgc	ctctcttgcc	2520
atagttttct	cctcctatat	cactcttggt	gtgctctttg	tgcccaagat	gcgcaggctg	2580
atcacccgag	gggaatggca	gtcggaggcg	caggacacca	tgaagacag	gtcatcgacc	2640
aacaaccaag	aggaggagaa	gtcccggctg	ttggagaagg	agaaccgtga	actggaaaag	2700
atcattgctg	agaaagagga	gcgtgtctct	gaactgcgcc	atcagctcca	gtctcggcag	2760
cagctccgct	cccggcgcca	cccaccgaca	cccccagaac	cctctggggg	cctgcccagg	2820
ggacccccctg	agccccccga	ccggcttagc	tgtgatggga	gtcagagtga	tttgctttat	2880



aagtgagggg	aggggtgaggg	aggacaggcc	agtaggggga	gggaaagggg	gaggggaagg	2940
gcaggggact	caggaagcag	gggggtcccca	tccccagctg	ggaagaacat	gctatccaat	3000
ctcatctctt	gtaaatacat	gtccccctgt	gagttctggg	ctgatttggg	tctctcatac	3060
ctctgggaaa	cagacctttt	tctctcttac	tgcttcatgt	aattttgtat	cacctcttca	3120
caatttagtt	cgtacctggc	ttgaagctgc	tcaactgcca	cacgctgcct	cctcagcagc	3180
ctcactgcat	ctttctcttc	ccatgcaaca	ccctcttcta	gttaccacgg	caacccctgc	3240
agctcctctg	cctttgtgct	ctgttctctg	ccagcagggg	tctcccaaca	agtgtctttt	3300
ccaccccaaa	ggggcctctc	cttttctcca	ctgtcataat	ctctttccat	cttacttgcc	3360
cttctatact	ttctcacatg	tggtctcccc	tgaattttgc	ttcctttggg	gagctcattc	3420
ntttcgccaa	ggntcacatg	ctcccttgcc	tctggctccg	tgca		3464

&lt;210&gt; 20

&lt;211&gt; 2887

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 20

atggggcccg	gggccccttt	tgcccgggtg	gggtggccac	tgccgcttct	ggttgtgatg	60
gcggcagggg	tggtccgggt	gtgggcctcc	cactccccc	atctcccgcg	gcctcactcg	120
cgggtccccc	cgcacccttc	ctcagaacgg	cgcgcagtgt	acatcggggc	actgtttccc	180
atgagcgggg	gctggccagg	ggggcaggcc	tgccagcccg	cgggtggagt	ggcgtggag	240
gacgtgaata	gccgcaggga	catcctgccg	gactatgagc	tcaagctcat	ccaccacgac	300
agcaagtgtg	atccaggcca	agccaccaag	tacctatatg	agctgctcta	caacgacctt	360
atcaagatca	tccttatgcc	tggttgagc	tctgtctcca	cgtgtggggc	tgaggctgct	420
aggatgtgga	acctcattgt	gctttcctat	ggctccagct	caccagccct	gtcaaaccgg	480
cagcgtttcc	ccactttctt	ccgaacgcac	ccatcagcca	cactccacaa	ccctaccgcg	540
gtgaaactct	ttgaaaagtg	gggctggaag	aagattgcta	ccatccagca	gaccactgag	600
gtcttcactt	cgactctgga	cgacctggag	gaacgagtga	aggaggctgg	aattgagatt	660
actttccgcc	agagtttctt	ctcagatcca	gctgtgcccg	tcaaaaacct	gaagcgccag	720
gatgcgccga	tcatcgtggg	acttttctat	gagactgaag	cccggaaaagt	tttttgtgag	780
gtgtacaagg	agcgtctctt	tggaagaag	tacgtctggt	tcctcattgg	gtggtatgct	840
gacaattggt	tcaagatcta	cgaccttct	atcaactgca	cagtggatga	gatgactgag	900
gcggtggagg	gccacatcac	aactgagatt	gtcatgctga	atcctgccaa	taccgcagc	960
atttccaaca	tgacatccca	ggaatttgtg	gagaaactaa	ccaagcgact	gaaaagacac	1020
cctgaggaga	caggaggctt	ccaggaggca	ccgctggcct	atgatgccat	ctgggccttg	1080
gcactggccc	tgaacaagac	atctggagga	ggcggccgtt	ctggtgtgcg	cctggaggac	1140
ttcaactaca	acaaccagac	cattaccgac	caaactctacc	gggcaatgaa	ctcttcgtcc	1200
tttgaggggtg	tctctggcca	tgtggtgttt	gatgccagcg	gctctcggt	ggcatggacg	1260
cttatcgagc	agcttcaggg	tggcagctac	aagaagattg	gctactatga	cagcaccgaag	1320
gatgatcttt	cctggtccaa	aacagataaa	tggtattggag	ggtccccccc	agctgaccag	1380
accctggtea	tcaagacatt	ccgcttcctg	tcacagaaac	tctttatctc	cgtctcagtt	1440
ctctccagcc	tgggcattgt	cctagctgtt	gtctgtctgt	cctttaacat	ctacaactca	1500
catgtccggt	atatccagaa	ctcacagccc	aacctgaaca	acctgactgc	tgtgggctgc	1560
tcactggctt	tagctgctgt	cttccccttg	gggtctgatg	gttaccacat	tgggaggaac	1620
cagtttcctt	tcgtctgcca	ggcccgcctc	tggtctctgg	gcctgggctt	tagtctgggc	1680
tacggttcca	tgttcaccaa	gatttgggtg	gtccacacgg	tcttcacaaa	gaaggaagaa	1740
aagaaggagt	ggaggaagac	tctggaaccc	tggaagctgt	atgccacagt	gggcctgctg	1800
gtgggcatgg	atgtcctcac	tctcgccatc	tggcagatcg	tggaacctct	gcaccggacc	1860
attgagacat	ttgccaaagga	ggaacctaa	gaagatattg	acgtctctat	tctgccccag	1920
ctggagcatt	gcagctccag	gaagatgaat	acatggcttg	gcattttcta	tggttacaa	1980
gggctgctgc	tgtgtctggg	aatcttcctt	gcttatgaga	ccaagagtgt	gtccactgag	2040
aagatcaatg	atcaccgggc	tgtgggcatg	gctatctaca	atgtggcagt	cctgtgcctc	2100

attgagacat	ttgccaagga	ggaacctaag	gaagatattg	acgtctctat	tctgccccag	1920
ctggagcatt	gcagctccag	gaagatgaat	acatggcttg	gcattttcta	tggttacaag	1980
gggctgctgc	tgctgctggg	aatcttccct	gcttatgaga	ccaagagtgt	gtccactgag	2040
aagatcaatg	atcaccgggc	tgtgggcatg	gctatctaca	atgtggcagt	cctgtgcctc	2100
atcactgctc	ctgtcaccat	gattctgtcc	agccagcagg	atgcagcctt	tgcccttgcc	2160
tctcttgcca	tagttttctc	ctcctatata	actcttggtg	tgctctttgt	gccccagatg	2220
cgcaggctga	tcacccgagg	ggaatggcag	tcggaggcgc	aggacaccat	gaagacaggg	2280
tcacgcacca	acaacaacga	ggaggagaag	tcccggctgt	tggaagaagg	gaaccgtgaa	2340
ctggaaaaga	tcattgctga	gaaagaggag	cgtgtctctg	aactgcgcca	tcaactccag	2400
tctcggcagc	agctccgctc	ccggcgccac	ccaccgacac	ccccagaacc	ctctgggggc	2460
ctgcccaggg	gacccctga	gccccccgac	cggcttagct	gtgatgggag	tcgagtgcac	2520
ttgctttata	agtgaaggta	gggtgaggga	ggacaggcca	gtagggggag	ggaaagggag	2580
aggggaaggg	caggggactc	aggaagcagg	gggtccccat	ccccagctgg	gaagaacatg	2640
ctatccaatc	tcattctctg	taaatacatg	tccccctgtg	agttctgggc	tgatttgggt	2700
ctctcatacc	tctgggaaac	agaccttttt	ctctcttact	gcttcatgta	atthttgtatc	2760
acctcttcac	aatttagttc	gtacctggct	tgaagctgct	cactgctcac	acgtgcctc	2820
ctcagcagcc	tcactgcata	tttctcttcc	catgcaacac	cctcttctag	ttaccacggc	2880
aacccct						2887

&lt;210&gt; 21

&lt;211&gt; 3144

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 21

atggcttccc	cgcggagctc	cgggcagccc	gggcccngc	cgcgcgcgc	accgcgcgc	60
gcgcgcctgc	tactgctact	gctgctgccc	ctgctgctgc	ctctggcgcc	cggggcctgg	120
ggctggggcg	ggggcgcccc	ccggccgcgc	cccagcagcc	cgcgcgtctc	catcatgggc	180
ctcatgcgcg	tcaccaagga	ggtggccaag	ggcagcatcg	ggcgcgggtg	gctccccgcc	240
gtggaactgg	ccatcgagca	gatccgcaac	gagtcactcc	tgccccccta	cttctctgac	300
ctgcggctct	atgacacgga	gtgcgacaac	gcaaaaagggt	tgaagcctt	ctacgatgca	360
ataaaatacg	ggccgaacca	cttgatgggtg	tttggaaggcg	tctgtccatc	cgtcacatcc	420
atcattgcag	agtcctctca	aggctggaat	ctggtgcagc	tttcttttgc	tgcaaccacg	480
cctgttctag	ccgataagaa	aaaataccct	tatttcttcc	ggaccgtccc	atcagacaat	540
gcggtgaatc	cagccattct	gaagtgtctc	aagcactacc	agtgggaagcg	cgtgggcacg	600
ctgacgcaag	acgttcagag	gttctctgag	gtgcggaatg	acctgactgg	agttctgtat	660
ggcgaggaca	ttgagatttc	agacaccgag	agcttctcca	acgatccctg	taccagtgtc	720
aaaaagctga	aggggaatga	tgtgcggatc	atccttgggc	agtttgacca	gaatatggca	780
gcaaaaagtgt	tctgttgtgc	atacaggagg	aacatgtatg	gtagtaaata	tcagtggatc	840
attccgggct	ggtacgagcc	ttcttggtgg	gagcaggtgc	acacggaagc	caactcatcc	900
cgctgcctcc	ggaagaatct	gcttgctgcc	atggagggct	acattggcgt	ggatttcgag	960
ccctgagct	ccaagcagat	caagaccatc	tcaggaaaga	ctccacagca	gtatgagaga	1020
gagtacaaca	acaagcggtc	aggcgtgggg	cccagcaagt	tccacgggta	cgcctacgat	1080
ggcatctggg	tcacgcgcaa	gacactgcag	agggccatgg	agacactgca	tgccagcagc	1140
cggcaccagc	ggatccagga	cttcaactac	acggaccaca	cgtcgggcag	gatcatcctc	1200
aatgccatga	acgagacca	cttcttcggg	gtcacgggtc	aagttgtatt	ccggaatggg	1260
gagagaatgg	ggaccattaa	atttactcaa	tttcaagaca	gcagggaggt	gaaggtggga	1320
gagtacaacg	ctgtggccga	cacactggag	atcatcaatg	acaccatcag	gttccaagga	1380
tccgaaccac	caaaagacaa	gaccatcatc	ctggagcagc	tgccggaagat	ctccctacct	1440
ctctacagca	tcctctctgc	cctcaccatc	ctcgggatga	tcattggccag	tgcttttctc	1500
ttcttcaaca	tcaagaaccg	gaatcagaag	ctcataaaga	tgtcaggtcc	atacatgaac	1560
aaccttatca	tccttgaggg	gatgctctcc	tatgcttcca	tatttctctt	tggccttgat	1620

tatgcctaca	agggacttct	catgttggtc	ggttggttct	tagcttgga	gacccgcaac	2040
gtcagcatcc	ccgcaactca	cgacagcaag	tacatcgga	tgagtgtcta	caacgtgggg	2100
atcatgtgca	tcatcggggc	cgctgtctcc	ttcctgaccc	gggaccagcc	caatgtgcag	2160
ttctgcatcg	tggtctctgt	catcatcttc	tgcagcacca	tcaccctctg	cctgggtattc	2220
gtgccgaagc	tcatcaccct	gagaacaaac	ccagatgcag	caacgcagaa	caggcgattc	2280
cagttcactc	agaatcagaa	gaaagaagat	tctaaaacgt	ccacctcggt	caccagtgtg	2340
aaccaagcca	gcacatcccg	cctggagggc	ctacagtcag	aaaaccatcg	cctgcgaatg	2400
aagatcacag	agctggataa	agacttgga	gaggtcacca	tgagctgca	ggacacacca	2460
gaaaagacca	cctacattaa	acagaaccac	taccaagagc	tcaatgacat	cctcaacctg	2520
ggaaacttca	ctgagagcac	agatggagga	aaggccattt	taaaaaatca	cctcgatcaa	2580
aatccccagc	tacagtggaa	cacaacagag	ccctctcgaa	catgcaaaga	tcctatagaa	2640
gatataaact	ctccagaaca	catccagcgt	cggtctgtcc	tccagctccc	catcctccac	2700
cacgcctacc	tcccatccat	cggaggcgtg	gacgccagct	gtgtcagccc	ctgcgtcagc	2760
cccaccgcca	gccccgcca	cagacatgtg	ccaccctcct	tccgagtcac	ggtctcgggc	2820
ctgttaagggt	gggaggcctg	ggcccggggc	ctcccccggt	acagaaccac	actgggcaga	2880
ggggctctgct	gcagaaacac	tgtcggctct	ggctgcggag	aagctgggca	ccatggctgg	2940
cctctcagga	ccactcggat	ggcactcagg	tggacaggac	ggggcagggg	gagacttggc	3000
acctgacctc	gagccttatt	tgtgaagtcc	ttatttcttc	acaaagaaga	ggaacggaaa	3060
tgggacgtct	tccttaacat	ctgcaaaaca	ggaggcgctg	ggatatcaaa	cttgcaaaaa	3120
aaaaaaaaa	aaaaaaaaa	aaaa				3144

&lt;210&gt; 22

&lt;211&gt; 2880

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 22

atgctgctgc	tgtgctggt	gcctctcttc	ctccgcccc	tgggcgctg	cggggcgcag	60
acccccaaag	ccacctcgga	agggtgccc	attatacatc	cgccctggga	agggtggcatc	120
aggtagcgtg	gcttgactcg	cgaccaggtg	aaggccatca	acttcctgcc	tgtggactat	180
gagatcgaat	atgtgtgccg	aggggagcgc	gaggtggtgg	ggcccaaggt	gcgcaaattgc	240
ctggccaacg	gctcctggac	ggatatggac	acaccagcc	gctgtgtccg	aatctgctcc	300
aagtcttatt	tgaccctgga	aaatgggaag	gttttccctga	cggttgggga	cctcccagct	360
ctggatggag	cccggttggg	gttccgatgt	gaacccgact	tccatctggt	gggcagctcc	420
cggagcgtct	gtagttaggg	ccagtggagc	acccccaaag	cccactgcca	ggtgaatcga	480
acgccacact	cagaacggcg	tgcagtatac	atcggggcgc	tggttcccat	gagcgggggc	540
tggccggggg	gccaggcctg	ccagcccgcg	gtggagatgg	cgctggagga	cgttaacagc	600
cgcagagaca	tcctgccgga	ctacgagctc	aagcttatcc	accacgacag	caagtgtgac	660
ccagggcaag	ccaccaagta	cttgtacgaa	ctactctaca	atgaccccat	caagatcatt	720
ctcatgctcg	gctgtagtgc	tgtctccaca	cttgtagctg	aggctgccc	gatgtggaac	780
cttattgtgc	tctcatatgg	ctccagttca	ccagccttgt	caaaccgaca	gcggtttccc	840
acgttcttcc	ggacgcaccc	atccgccaca	ctccacaatc	ccaccgggtg	gaaactcttc	900
gaaaagtggg	gctggaagaa	gatcgctacc	atccaacaga	ccaccgaggt	cttcacctca	960
acgttgatg	acctggagga	gcgagtgaag	gaggttggga	tcgagatcac	tttccgacag	1020
agtttcttct	cggatccagc	tgtgcctgtt	aaaaacctga	agcgtcaaga	tgtctgaatc	1080
atcgtgggac	ttttctatga	gacggaagcc	cggaaagtgt	tttgtgaggt	ctataaggaa	1140
aggctctttg	ggaagaagta	cgtctggttc	ctcatcggtg	ggtatgctga	caactggttc	1200
aagacctatg	acccgtcaat	caattgtaca	gtggaagaaa	tgaccgaggc	ggtggagggc	1260
cacatcacca	cggagattgt	catgctgaac	cctgccaaaca	cccgaagcat	ttccaacatg	1320
acgtcacagg	aatttgtgga	gaaactaacc	aagcggctga	aaagacaccc	cgaggagact	1380
ggaggcttcc	aggaggcacc	actggcctat	gatgctatct	gggccttgcc	tttggccttg	1440
aacaagacgt	ctggaggagg	tggctgttcc	ggcgtgcgcc	tggaggactt	taactacaac	1500
aaccagacca	ttacagacca	gatctaccgg	gccatgaact	cctcctcctt	tgagggcgtt	1560

tctggccatg	tggtctttga	tgccagcggc	tcccggatgg	catggacact	tatcgagcag	1620
ctacagggcg	gcagctacaa	gaagatcggc	tactacgaca	gcaccaagga	tgatctttcc	1680
tggtccaaaa	cggacaagtg	gattggaggg	tctcccccag	ctgaccagac	cttggtcatc	1740
aagacattcc	gtttcctgtc	tcagaaactc	tttatctccg	tctcagttct	ctccagcctg	1800
ggcattgttc	ttgctgttgt	ctgtctgtcc	tttaacatct	acaactccca	cgttcgttat	1860
atccagaact	cccagcccaa	cctgaacaat	ctgactgctg	tgggctgctc	actggcactg	1920
gctgctgtct	tccctctcgg	gctggatggg	taccacatag	ggagaagcca	gttcccgttt	1980
gtctgccagg	cccgcccttg	gctcttgggc	ttgggcttta	gtctgggcta	tggtctctatg	2040
ttcaccaaga	tctggtggtg	ccacacagtc	ttcacgaaga	aggaggagaa	gaaggagtgg	2100
aggaagacct	tagagccctg	gaaactctat	gccactgtgg	gcctgctggt	gggcatggat	2160
gtectgactc	ttgccatctg	gcagattgtg	gaccccttgc	accgaacctt	tgagactttt	2220
gccaaaggag	aaccaaagga	agacatcgat	gtctccattc	tgccccagtt	ggagcactgc	2280
agctccaaga	agatgaatac	gtggcttggc	attttctatg	gttacaaggg	gctgctgctg	2340
ctgctgggaa	tctttcttgc	ttacgaaacc	aagagcgtgt	ccactgaaaa	gatcaatgac	2400
cacaggcccg	tgggcatggc	tatctacaat	gtcgcggtcc	tgtgtctcat	cactgctcct	2460
gtgaccatga	tcctttccag	tcagcaggac	gcagcctttg	cctttgcctc	tctggccatc	2520
gtgttctctt	cctacatcac	tctggttgtg	ctctttgtgc	ccaagatgcg	caggctgatc	2580
acccgagggg	aatggcagtc	tgaaacgcag	gacaccatga	aaacaggatc	atccaccaac	2640
aacaacgagg	aagagaagtc	ccgactgttg	gagaaggaaa	accgagaact	ggaaaagatc	2700
atcgctgaga	aagaggagcg	cgtctctgaa	ctgcgccatc	agctccagtc	tcggcagcaa	2760
ctcgcgtcac	ggcgccaccc	cccaacaccc	ccagatccct	ctgggggcct	tcccagggga	2820
ccctctgagc	cccctgaccg	gcttagctgt	gatgggagtc	gagtacattt	gctttacaag	2880

&lt;210&gt; 23

&lt;211&gt; 2532

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 23

atggggcccg	ggggaccctg	taccccagtg	gggtggccgc	tgcctcttct	gctggtgatg	60
gcggctgggg	tggtctccgt	gtgggcctct	cactcccctc	atctcccgcg	gcctcaccgc	120
agggctcccc	cgcacccctc	ctcagaacgg	cgtgcagtat	acatcggggc	gctgtttccc	180
atgagcgggg	gctggccggg	gggcccaggc	tgccagcccg	cggtggagat	ggcgctggag	240
gacgttaaca	gocgcagaga	catcctgccc	gactacgagc	tcaagcttat	ccaccacgac	300
agcaagtgtg	acccagggca	agccaccaag	tacttgtagc	aactactcta	caatgacccc	360
atcaagatca	ttctcatgcc	tggtgttagt	tctgtctcca	cacttgtagc	tgaggctgcc	420
cggatgtgga	accttattgt	gctctcatat	ggctccagtt	caccagcctt	gtcaaaccga	480
cagcggtttc	ccacgttctt	ccggacgcat	ccatccgcca	cactccacaa	tcccacccgg	540
gtgaaaactc	tcgaaaagtg	gggctggaag	aagatcgcta	ccatccaaca	gaccaccgag	600
gtcttcacct	caacgctgga	tgacctggag	gagcgagtga	aagaggctgg	gatcgagatc	660
actttccgac	agagtttctt	ctcggtacca	gctgtgcctg	ttaaaaacct	gaagcgtaaa	720
gatgctcgaa	tcatcgtggg	acttttctat	gagacggaag	cccggaaaagt	tttttgtgag	780
gtctataaag	aaaggctctt	tggaagaag	tacgtctggt	tcctcatcgg	gtggtatgct	840
gacaactggt	tcaagacctt	tgacctgtca	atcaattgta	cagtggaaag	aatgaccgag	900
gcgggtggagg	gccacatcac	cacggagatt	gtcatgctga	accctgccaa	caccggaagc	960
atttccaaca	tgacgtcaca	ggaatttgtg	gagaaactaa	ccaagcggct	gaaaagacac	1020
ccgagtgaga	ctggaggctt	ccaggaggca	ccactggcct	atgatgctat	ctgggccttg	1080
gctttggcct	tgaacaagac	gtctggagga	ggtggtcggt	ccggcggtgcg	cctggaggac	1140
tttaactaca	acaaccagac	cattacagac	cagatctacc	gggccatgaa	ctcctcctcc	1200
tttgagggcg	tttctggcca	tgtggtcttt	gatgccagcg	gctcccggat	ggcatggaca	1260
cttatcgagc	agctacaggg	cggcagctac	aagaagatcg	gctactacga	cagcaccaag	1320

```

gatgatcttt cctgggtccaa aacggacaag tggattggag ggtctccccc agctgaccag 1380
accttgggtca tcaagacatt ccgtttcctg tctcagaaac tctttatctc cgtctcagtt 1440
ctctccagcc tgggcattgt tcttgtctgt gtctgtctgt cctttaacat ctacaactcc 1500
cacgttcgtt atatccagaa ctcccagccc aacctgaaca atctgactgc tgtgggctgc 1560
tcaactggcac tggctgctgt cttccctctc gggctggatg gttaccacat agggagaagc 1620
cagttcccgt ttgtctgcca ggcccgcctt tggctcttgg gcttgggctt tagtctgggc 1680
tatggctcta tgttcaccaa gatctgggtg gtccacacag tcttcacgaa gaaggaggag 1740
aagaaggagt ggaggaagac cctagagccc tggaaactct atgccactgt gggcctgctg 1800
gtgggcatgg atgtcctgac tcttgccatc tggcagattg tggaccctt gcaccgaacc 1860
attgagactt ttgccaagga ggaaccaaag gaagacatcg atgtctccat tctgccccag 1920
ttggagcact gcagctccaa gaagatgaat acgtggcttg gcattttcta tggttacaag 1980
gggtgctgctg tgcgtgctggg aatctttctt gcttacgaaa ccaagagcgt gtccactgaa 2040
aagatcaatg accacagggc cgtgggcatg gctatctaca atgtcgcggt cctgtgtctc 2100
atcactgctc ctgtgacct gatcctttcc agtcagcagg acgcagcctt tgcctttgcc 2160
tctctggcca tgcgtgtctc ttcctacatc actctggttg tgcctttgt gcccaagatg 2220
cgcaggctga tcacccgagg ggaatggcag tctgaaacgc aggacaccat gaaaacagga 2280
tcatccacca acaacaacga ggaagagaag tcccagactgt tggagaagga aaaccgagaa 2340
ctggaanaa tcatcgtga gaaagaggag cgcgtctctg aactgcgcca tcagctccag 2400
tctcggcagc aactccgctc acggcgccac ccccaaacac cccagatcc ctctgggggc 2460
cttcccaggg gacctctga gcccctgac cggcttagct gtgatgggag tcgagtacat 2520
ttgctttaca ag 2532

```

<210> 24  
 <211> 960  
 <212> PRT  
 <213> Rat

<400> 24

```

Met Leu Leu Leu Leu Leu Val Pro Leu Phe Leu Arg Pro Leu Gly Ala
 1             5             10            15

Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile Ile
 20             25            30

His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg Asp
 35             40            45

Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu Tyr
 50             55            60

Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys Cys
 65             70            75            80

Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys Val
 85             90            95

Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val Phe
100            105            110

Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Glu Phe
115            120            125

```

Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Val Cys  
 130 135 140  
 Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn Arg  
 145 150 155 160  
 Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro  
 165 170 175  
 Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu  
 180 185 190  
 Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr  
 195 200 205  
 Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala  
 210 215 220  
 Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile  
 225 230 235 240  
 Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala  
 245 250 255  
 Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala  
 260 265 270  
 Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser  
 275 280 285  
 Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly  
 290 295 300  
 Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser  
 305 310 315 320  
 Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile  
 325 330 335  
 Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn  
 340 345 350  
 Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr  
 355 360 365  
 Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly  
 370 375 380  
 Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe  
 385 390 395 400  
 Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu  
 405 410 415

Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala  
 420 425 430  
 Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys  
 435 440 445  
 Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln  
 450 455 460  
 Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu  
 465 470 475 480  
 Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp  
 485 490 495  
 Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met  
 500 505 510  
 Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala  
 515 520 525  
 Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly  
 530 535 540  
 Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser  
 545 550 555 560  
 Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln  
 565 570 575  
 Ile Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile  
 580 585 590  
 Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys  
 595 600 605  
 Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser  
 610 615 620  
 Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu  
 625 630 635 640  
 Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser  
 645 650 655  
 Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly  
 660 665 670  
 Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His  
 675 680 685  
 Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu  
 690 695 700

33

Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp  
 705 710 715 720  
 Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr  
 725 730 735  
 Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser  
 740 745 750  
 Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp  
 755 760 765  
 Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile  
 770 775 780  
 Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp  
 785 790 795 800  
 His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu  
 805 810 815  
 Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala  
 820 825 830  
 Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu  
 835 840 845  
 Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu  
 850 855 860  
 Trp Gln Ser Glu Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn  
 865 870 875 880  
 Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu  
 885 890 895  
 Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg  
 900 905 910  
 His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro  
 915 920 925  
 Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro  
 930 935 940  
 Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys  
 945 950 955 960

<210> 25  
 <211> 844  
 <212> PRT  
 <213> Rat



&lt;400&gt; 25

Met Gly Pro Gly Gly Pro Cys Thr Pro Val Gly Trp Pro Leu Pro Leu  
 1 5 10 15  
 Leu Leu Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser  
 20 25 30  
 Pro His Leu Pro Arg Pro His Pro Arg Val Pro Pro His Pro Ser Ser  
 35 40 45  
 Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly  
 50 55 60  
 Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu  
 65 70 75 80  
 Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu  
 85 90 95  
 Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu  
 100 105 110  
 Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly  
 115 120 125  
 Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn  
 130 135 140  
 Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg  
 145 150 155 160  
 Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His  
 165 170 175  
 Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile  
 180 185 190  
 Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp  
 195 200 205  
 Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln  
 210 215 220  
 Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln  
 225 230 235 240  
 Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys  
 245 250 255  
 Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val  
 260 265 270

Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Thr Tyr Asp  
 275 280 285  
 Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu Ala Val Glu Gly  
 290 295 300  
 His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser  
 305 310 315 320  
 Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg  
 325 330 335  
 Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu  
 340 345 350  
 Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser  
 355 360 365  
 Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn  
 370 375 380  
 Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser  
 385 390 395 400  
 Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg  
 405 410 415  
 Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys  
 420 425 430  
 Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr  
 435 440 445  
 Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Ile Leu Val Ile  
 450 455 460  
 Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val  
 465 470 475 480  
 Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn  
 485 490 495  
 Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu  
 500 505 510  
 Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe  
 515 520 525  
 Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser Gln Phe Pro Phe  
 530 535 540  
 Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly  
 545 550 555 560

Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr  
 565 570 575  
 Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys  
 580 585 590  
 Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu  
 595 600 605  
 Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe  
 610 615 620  
 Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln  
 625 630 635 640  
 Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp Leu Gly Ile Phe  
 645 650 655  
 Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr  
 660 665 670  
 Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val  
 675 680 685  
 Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro  
 690 695 700  
 Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala  
 705 710 715 720  
 Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe  
 725 730 735  
 Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu  
 740 745 750  
 Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu  
 755 760 765  
 Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile  
 770 775 780  
 Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln  
 785 790 795 800  
 Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Asp  
 805 810 815  
 Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro Pro Asp Arg Leu  
 820 825 830  
 Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys  
 835 840

<210> 26  
 <211> 2616  
 <212> DNA  
 <213> Human

<400> 26

atgggatcgc	tgcttgcgct	cctggcactg	ctgccgctgt	ggggtgctgt	ggctgagggc	60
ccagccaaga	aggtgctgac	cctggaggga	gacttggtgc	tgggtgggct	gttcccagtg	120
caccagaagg	gcggcccagc	agaggactgt	ggctctgtca	atgagcaccg	tggcatccag	180
cgcctggagg	ccatgctttt	tgcactggac	cgcatacaacc	gtgacccgca	cctgctgcct	240
ggcgtgcgcc	tgggtgcaca	catcctcgac	agttgctcca	aggacacaca	tgcgctggag	300
caggcactgg	actttgtgcg	tgcctcactc	agccgtgggt	ctgatggatc	acgccacatc	360
tgccccgacg	gctcttatgc	gacccatggt	gatgctccca	ctgccatcac	tgggtgttatt	420
ggcggttcct	acagtgatgt	tcccatccag	gtggccaacc	tcttgaggct	atttcagatc	480
ccacagatta	gctacgcctc	taccagtgcc	aagctgagtg	acaagtcccg	ctatgactac	540
tttgccccga	cagtgcctcc	tgacttcttc	caagccaagg	ccatggctga	gattctccgc	600
ttcttcaact	ggacctatgt	gtccactgag	gcctctgagg	gcgactatgg	cgagacaggc	660
attgaggcct	ttgagctaga	ggctcgtgcc	cgcaacatct	gtgtggccac	ctcggagaaa	720
gtgggccgtg	ccatgagccg	cgcggccttt	gaggggtgtg	tgcgagccct	gctgcagaag	780
cccagtgcct	gcgtggctgt	cctgttcacc	cggtctgagg	atgcccgga	gctgcttgct	840
gccagccagc	gcctcaatgc	cagcttcacc	tgggtggcca	gtgatgggtg	gggggccctg	900
gagagtgtgg	tggcaggcag	tgagggggct	gctgaggggt	ctatcaccat	cgagctggcc	960
tcctacccca	tcagtgaact	tgcctcctac	ttccagagcc	tggacccttg	gaacaacagc	1020
cggaaaccct	ggttcctgta	attctgggag	cagagggtcc	gctgcagctt	ccggcagcga	1080
gactgcgcag	cccactctct	ccgggctgtg	ccctttgaac	aggagtccaa	gatcatgttt	1140
gtggtcaatg	cagtgtacgc	catggcccat	gcgctccaca	acatgcaccg	tgcctctgc	1200
cccaacacca	ccgggtcttg	tgacgcgatg	cggccagtta	acgggcgccc	cctctacaag	1260
gactttgtgc	tcaacgtcaa	gtttgatgcc	ccctttcgcc	cagctgacac	ccacaatgag	1320
gtccgctttg	accgctttgg	tgatggattt	ggccgctaca	acatcttcac	ctatctgcgt	1380
gcaggcagtg	ggcgctatcg	ctaccagaag	gtgggctact	gggcagaagg	cttgactctg	1440
gacaccagcc	tcattccatg	ggcctcaccg	tcagccggcc	ccctggccgc	ctctcgctgc	1500
agtgaaccct	gcctccagaa	tgagggtgaag	agtgtgcagc	cgggcgaagt	ctgctgctgg	1560
ctctgcattc	cgtgccagcc	ctatgagtac	cgattggacg	aattcacttg	cgctgattgt	1620
ggcctgggct	actggcccaa	tgccagcctg	actggctgct	tcgaactgcc	ccaggagta	1680
atccgctggg	gcgatgcctg	ggctgtggga	cctgtcacca	tgcctgcct	cgggtgccctg	1740
gccaccctgt	ttgtgctggg	tgtctttgtg	cggcacaatg	ccacaccagt	ggtcaaggcc	1800
tcaggtcggg	agctctgcta	catcctgctg	ggtggtgtct	tcctctgcta	ctgcattgacc	1860
ttcatcttca	ttgccaaagc	atccacggca	gtgtgtacct	tacggcgtct	tggtttgggc	1920
actgccttct	ctgtctgcta	ctcagccctg	ctcaccaaga	ccaaccgcat	tgcacgcctc	1980
ttcgggtggg	cccgggaggg	tgccagcgcg	ccacgcttca	tcagtcctgc	ctcacagggtg	2040
gccatctgcc	tggcacttat	ctcgggccag	ctgctcatcg	tggctgcctg	gctgggtgggt	2100
gaggcaccgg	gcacaggcaa	ggagacagcc	cccgaacggc	gggaggtggg	gacactgcgc	2160
tgcaaccacc	gcgatgcaag	tatgttgggc	tcgctggcct	acaatgtgct	cctcatcgcg	2220
ctctgcacgc	tttatgcctt	caatactcgc	aagtgcctcg	aaaacttcaa	cgaggccaag	2280
ttcattggct	tcaccatgta	caccacctgc	atcatctggc	tggcattgtt	gcccatcttc	2340
tatgtcacct	ccagtgacta	ccgggtacag	accaccacca	tgtgcgtgtc	agtcagcctc	2400
agcggctccg	tgggtgcttg	ctgcctcttt	gcgcccaagc	tgcacatcat	cctcttccag	2460
ccgcagaaga	acgtgggttag	ccaccgggca	cccaccagcc	gctttggcag	tgtgctgccc	2520
agggccagct	ccagccttgg	ccaagggtct	ggctcccagt	ttgtccccat	tgtttgcaat	2580
ggcctgtagg	tgggtggactc	gacaacgtca	tcgctt			2616

38

<210> 27  
 <211> 824  
 <212> PRT  
 <213> Human

<400> 27

Met Gly Ser Leu Leu Ala Leu Leu Ala Leu Leu Pro Leu Trp Gly Ala  
 1 5 10 15

Val Ala Glu Gly Pro Ala Lys Lys Val Leu Thr Leu Glu Gly Asp Leu  
 20 25 30

Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu  
 35 40 45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala  
 50 55 60

Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro  
 65 70 75 80

Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr  
 85 90 95

His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg  
 100 105 110

Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr  
 115 120 125

His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr  
 130 135 140

Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile  
 145 150 155 160

Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser  
 165 170 175

Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala  
 180 185 190

Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser  
 195 200 205

Thr Glu Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe  
 210 215 220

Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys  
 225 230 235 240

Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala  
 245 250 255

39

Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser  
 260 265 270  
 Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser  
 275 280 285  
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val  
 290 295 300  
 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala  
 305 310 315 320  
 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro  
 325 330 335  
 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg  
 340 345 350  
 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg  
 355 360 365  
 Ala Val Pro Phe Glu Gln Glu Ser Lys Ile Met Phe Val Val Asn Ala  
 370 375 380  
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys  
 385 390 395 400  
 Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg  
 405 410 415  
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe  
 420 425 430  
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp  
 435 440 445  
 Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly  
 450 455 460  
 Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu  
 465 470 475 480  
 Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Ala  
 485 490 495  
 Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val  
 500 505 510  
 Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr  
 515 520 525  
 Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr  
 530 535 540

40

Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr  
 545 550 555 560  
 Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys  
 565 570 575  
 Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His  
 580 585 590  
 Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile  
 595 600 605  
 Leu Leu Gly Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile  
 610 615 620  
 Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly  
 625 630 635 640  
 Thr Ala Phe Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg  
 645 650 655  
 Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg  
 660 665 670  
 Phe Ile Ser Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser  
 675 680 685  
 Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly  
 690 695 700  
 Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg  
 705 710 715 720  
 Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val  
 725 730 735  
 Leu Leu Ile Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys  
 740 745 750  
 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr  
 755 760 765  
 Thr Cys Ile Ile Trp Leu Ala Leu Leu Pro Ile Phe Tyr Val Thr Ser  
 770 775 780  
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu  
 785 790 795 800  
 Ser Gly Ser Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile  
 805 810 815  
 Ile Leu Phe Gln Pro Gln Lys Asn  
 820

41

<210> 28  
 <211> 1077  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Chimeric Gqi5

<400> 28

```

atgactctgg agtccatcat ggcgtgctgc ctgagcgagg aggccaagga agccccggcg      60
atcaacgacg agatcgagcg gcagctccgc agggacaagc gggacgcccg ccgggagctc      120
aagctgctgc tgctcgggac aggagagagt ggcaagagta cgtttatcaa gcagatgaga      180
atcatccatg ggtcaggata ctctgatgaa gataaaaggg gcttcaccaa gctggtgtat      240
cagaacatct tcacggccat gcaggccatg atcagagcca tggacacact caagatccca      300
tacaagtatg agcacaataa ggctcatgca caattagttc gagaagttga tgtggagaag      360
gtgtctgctt ttgagaatcc atatgtagat gcaataaaga gtttatggaa tgatcctgga      420
atccaggaat gctatgtag acgacgagaa tatcaattat ctgactctac caaatactat      480
cttaaatgact tggaccgctg agctgacct gcctacctgc ctacgcaaca agatgtgctt      540
agagtctcag tccccaccac agggatcatc gaatacccct ttgacttaca aagtgtcatt      600
ttcagaatgg tcgatgtagg gggccaaagg tcagagagaa gaaaatggat aactgtcttt      660
gaaaatgtca cctctatcat gtttctagta gcgcttagtg aatatgatca agttctcgtg      720
gagtcagaca atgagaaccg aatggaggaa agcaaggctc tctttagaac aattatcaca      780
tacccttggt tccagaactc ctcggttatt ctgttcttaa acaagaaaga tcttctagag      840
gagaaaatca tgtattccca tctagtgcac tacttcccag aatatgatgg accccagaga      900
gatgcccgag cagcccgaga attcattctg aagatgttcg tggacctgaa cccagacagt      960
gacaaaatta tctactccca cttcacgtgc gccacagaca ccgagaatat ccgctttgtc     1020
tttgctgccc tcaaggacac catcctccag ttgaacctga aggactgccc tctgttc      1077

```

<210> 29  
 <211> 359  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Chimeric Gqi5

<400> 29

```

Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu Ser Glu Glu Ala Lys
 1              5              10              15

Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu Arg Arg Asp
 20              25              30

Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Gly Thr Gly
 35              40              45

Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly
 50              55              60

Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr
 65              70              75              80

```



42

Gln Asn Ile Phe Thr Ala Met Gln Ala Met Ile Arg Ala Met Asp Thr  
 85 90 95  
 Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His Ala Gln Leu  
 100 105 110  
 Val Arg Glu Val Asp Val Glu Lys Val Ser Ala Phe Glu Asn Pro Tyr  
 115 120 125  
 Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly Ile Gln Glu Cys  
 130 135 140  
 Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser Thr Lys Tyr Tyr  
 145 150 155 160  
 Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr Leu Pro Thr Gln  
 165 170 175  
 Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr Gly Ile Ile Glu Tyr  
 180 185 190  
 Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met Val Asp Val Gly Gly  
 195 200 205  
 Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu Asn Val Thr  
 210 215 220  
 Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln Val Leu Val  
 225 230 235 240  
 Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg  
 245 250 255  
 Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val Ile Leu Phe  
 260 265 270  
 Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr Ser His Leu  
 275 280 285  
 Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp Ala Gln Ala  
 290 295 300  
 Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn Pro Asp Ser  
 305 310 315 320  
 Asp Lys Ile Ile Tyr Ser His Phe Thr Cys Ala Thr Asp Thr Glu Asn  
 325 330 335  
 Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr Ile Leu Gln Leu Asn  
 340 345 350  
 Leu Lys Asp Cys Gly Leu Phe  
 355

<210> 30  
 <211> 2751  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Chimeric hCAR/hmGluR2

<400> 30

atggcatttt	atagctgctg	ctgggtcctc	ttggcactca	cctggcacac	ctctgcttac	60
gggccagacc	agcgagccca	aaagaagggg	gacattatcc	ttgggggggt	ctttccctatt	120
catttttgag	tagcagctaa	agatcaagat	ctcaaataca	ggccggagtc	tgtggaatgt	180
atcaggtata	atttcctgtg	gtttcgtctg	ttacaggcta	tgatatttgc	catagaggag	240
ataaacagca	gcccagccct	tcttcccaac	ttgacgctgg	gatacaggat	atttgacact	300
tgaacacccg	tttctaagcg	cttggaaagc	accctgagtt	ttgttgctca	aaacaaaatt	360
gattctttga	accttgatga	gttctgcaac	tgtcagagc	acattccctc	tacgattgct	420
gtggtgggag	caactggctc	aggcgtctcc	acggcagtg	caaactctgt	ggggctcttc	480
tacattcccc	aggtcagtta	tgcctcctcc	agcagactcc	tcagcaacaa	gaatcaattc	540
aagtctttcc	tccgaacccat	ccccaatgat	gagcaccagg	ccactgccat	ggcagacatc	600
atcgagtatt	tccgctggaa	ctgggtgggc	acaattgcag	ctgatgacga	ctatgggcgg	660
ccggggattg	agaaattccg	agaggaagct	gaggaagagg	atatctgcat	cgacttcagt	720
gaactcatct	cccagtactc	tgatgaggaa	gagatccagc	atgtggtaga	ggtgattcaa	780
aattccacgg	ccaaagtcac	cgtgggtttc	tccagtggcc	cagatcttga	gccccctcatc	840
aaggagattg	tccggcgcaa	tatcacgggc	aagatctggc	tggccagcga	ggcctggggcc	900
agctcctccc	tgatcgccat	gcctcagtac	ttccacgtgg	ttggcggcac	cattggattc	960
gctctgaagg	ctgggcagat	cccaggcttc	cgggaattcc	tgaagaaggt	ccatcccagg	1020
aagtctgtcc	acaatggttt	tgccaaggag	ttttgggaag	aaacatttaa	ctgccacctc	1080
caagaagggt	caaaaggacc	tttacctgtg	gacacctttc	tgagaggtca	cgaagaaagt	1140
ggcgacaggt	ttagcaacag	ctcgacagcc	ttccgacccc	tctgtacagg	ggatgagaac	1200
atcagcagtg	tcgagacccc	ttacatagat	tacacgcatt	tacggataatc	ctacaatgtg	1260
tacttagcag	tctactccat	tgcccacgcc	ttgcaagata	tatatacctg	cttacctggg	1320
agagggctct	tcaccaatgg	ctcctgtgca	gacatcaaga	aagttgaggc	gtggcaggtc	1380
ctgaagcacc	tacggcatct	aaactttaca	aacaatatgg	gggagcaggt	gacctttgat	1440
gagtgtggtg	acctgggtgg	gaactattcc	atcatcaact	ggcacctctc	cccagaggat	1500
ggctccatcg	tgtttaagga	agtccgggtat	tacaacgtct	atgccaaaga	gggagaaaga	1560
ctcttcatca	acgaggagaa	aatcctgtgg	agtgggttct	ccaggggaggt	gcccttcttc	1620
aactgcagcc	gagactgcct	ggcagggacc	aggaaaggga	tcattgaggg	ggagcccacc	1680
tgctgctttg	agtgtgtgga	gtgtcctgat	ggggagtata	gtgatgagac	agatgccagt	1740
gcctgtaaca	agtgcccaga	tgacttctgg	tccaatgaga	accacacctc	ctgcttcgaa	1800
ctgccccagg	agtacatccg	ctggggcgat	gcctgggctg	tgggacctgt	caccatcgcc	1860
tgcctcgggtg	ccctggccac	cctgttttgt	ctgggtgtct	ttgtgcggca	caatgccaca	1920
ccagtggtca	aggcctcagg	tcgggagctc	tgtacatcc	tgtcgggtgg	tgtcttctctc	1980
tgtactgca	tgaccttcat	cttcattgcc	aagccatcca	cggcagtggtg	taccttacgg	2040
cgtcttggtt	tgggcaactgc	cttctctgtc	tgtactcag	ccctgctcac	caagaccaac	2100
cgcatcgcac	gcatcttcgg	tggggcccgg	gaggggtgcc	agcggccacg	cttcacagtc	2160
cctgcctcac	aggtggccat	ctgcctggca	cttatctcgg	gccagctgct	catcgtggtc	2220
gcctggctgg	tgggtggaggc	accgggcaca	ggcaaggaga	cagccccga	acggcgggag	2280
gtggtgacac	tgcgctgcaa	ccaccgcgat	gcaagtatgt	tgggtctcgt	ggcctacaat	2340
gtgctectca	tcgcgctctg	cacgctttat	gccttcaata	ctcgcaagtg	ccccgaaaac	2400
ttcaacgagg	ccaagtccat	tggcttcacc	atgtacacca	cctgcatcat	ctggctggca	2460
ttgttgccca	tcttctatgt	cacctccagt	gactaccggg	tacagaccac	caccatgtgc	2520
gtgtcagtc	gcctcagcgg	ctccgtgggtg	cttggtgtgc	tctttgcgcc	caagctgcac	2580
atcctcctct	tccagccgca	gaagaacgtg	gttagccacc	gggcacccac	cagccgcttt	2640

```

ggcagtgtctg ctgccagggc cagctccagc cttggccaag ggtctggctc ccagtttgtc 2700
cccactgttt gcaatggccg tgaggtgggtg gactcgacaa cgtcatcgct t 2751

```

```

<210> 31
<211> 917
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Chimeric hCAR/hmGluR2

```

```

<400> 31

```

```

Met Ala Phe Tyr Ser Cys Cys Trp Val Leu Leu Ala Leu Thr Trp His
 1             5             10             15

Thr Ser Ala Tyr Gly Pro Asp Gln Arg Ala Gln Lys Lys Gly Asp Ile
      20             25             30

Ile Leu Gly Gly Leu Phe Pro Ile His Phe Gly Val Ala Ala Lys Asp
      35             40             45

Gln Asp Leu Lys Ser Arg Pro Glu Ser Val Glu Cys Ile Arg Tyr Asn
      50             55             60

Phe Arg Gly Phe Arg Trp Leu Gln Ala Met Ile Phe Ala Ile Glu Glu
      65             70             75             80

Ile Asn Ser Ser Pro Ala Leu Leu Pro Asn Leu Thr Leu Gly Tyr Arg
      85             90             95

Ile Phe Asp Thr Cys Asn Thr Val Ser Lys Ala Leu Glu Ala Thr Leu
      100            105            110

Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe
      115            120            125

Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala
      130            135            140

Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe
      145            150            155            160

Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Ser Arg Leu Leu Ser Asn
      165            170            175

Lys Asn Gln Phe Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His
      180            185            190

Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp
      195            200            205

```

45

Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu  
 210 215 220  
 Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser  
 225 230 235 240  
 Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val  
 245 250 255  
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser  
 260 265 270  
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile  
 275 280 285  
 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu  
 290 295 300  
 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe  
 305 310 315 320  
 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys  
 325 330 335  
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp  
 340 345 350  
 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu  
 355 360 365  
 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe  
 370 375 380  
 Ser Asp Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn  
 385 390 395 400  
 Ile Ser Ser Val Glu Thr Pro Tyr Ile Asp Tyr Thr His Leu Arg Ile  
 405 410 415  
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln  
 420 425 430  
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser  
 435 440 445  
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu  
 450 455 460  
 Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp  
 465 470 475 480  
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu  
 485 490 495

Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn  
 500 505 510  
 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile  
 515 520 525  
 Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg  
 530 535 540  
 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr  
 545 550 555 560  
 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu  
 565 570 575  
 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn  
 580 585 590  
 Glu Asn His Thr Ser Cys Phe Glu Leu Pro Gln Glu Tyr Ile Arg Trp  
 595 600 605  
 Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys Leu Gly Ala  
 610 615 620  
 Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His Asn Ala Thr  
 625 630 635 640  
 Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile Leu Leu Gly  
 645 650 655  
 Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile Ala Lys Pro  
 660 665 670  
 Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly Thr Ala Phe  
 675 680 685  
 Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg Ile Ala Arg  
 690 695 700  
 Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg Phe Ile Ser  
 705 710 715 720  
 Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser Gly Gln Leu  
 725 730 735  
 Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly Thr Gly Lys  
 740 745 750  
 Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg Cys Asn His  
 755 760 765  
 Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val Leu Leu Ile  
 770 775 780

47

Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys Pro Glu Asn  
 785 790 795 800

Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr Thr Cys Ile  
 805 810 815

Ile Trp Leu Ala Leu Leu Pro Ile Phe Tyr Val Thr Ser Ser Asp Tyr  
 820 825 830

Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu Ser Gly Ser  
 835 840 845

Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile Ile Leu Phe  
 850 855 860

Gln Pro Gln Lys Asn Val Val Ser His Arg Ala Pro Thr Ser Arg Phe  
 865 870 875 880

Gly Ser Ala Ala Ala Arg Ala Ser Ser Ser Leu Gly Gln Gly Ser Gly  
 885 890 895

Ser Gln Phe Val Pro Thr Val Cys Asn Gly Arg Glu Val Val Asp Ser  
 900 905 910

Thr Thr Ser Ser Leu  
 915

&lt;210&gt; 32

&lt;211&gt; 3831

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Chimeric phCaR/hmGluR2\*Gqi5

&lt;400&gt; 32

atggcatttt	atagctgctg	ctgggtcctc	ttggcactca	cctggcacac	ctctgcctac	60
gggccagacc	agcgagccca	aaagaagggg	gacattatcc	ttggggggct	ctttcctatt	120
cattttggag	tagcagctaa	agatcaagat	ctcaaatcaa	ggccggagtc	tgtggaatgt	180
atcaggtata	atttccgtgg	gtttcgctgg	ttacaggcta	tgatatttgc	catagaggag	240
ataaacagca	gcccagccct	tcttcccaac	ttgacgctgg	gatacaggat	atttgacact	300
tgcaacaccg	tttctaaggc	cttgggaagcc	accctgagtt	ttgttgctca	aaacaaaatt	360
gattctttga	accttgatga	gttctgcaac	tgctcagagc	acattccctc	tacgattgct	420
gtggtgggag	caactggctc	aggcgtctcc	acggcagtg	caaatctgct	ggggctcttc	480
tacattcccc	aggtcagtta	tgctcctctc	agcagactcc	tcagcaacaa	gaatcaattc	540
aagtctttcc	tccgaaccat	ccccaatgat	gagcaccagg	ccactgccat	ggcagacatc	600
atcgagtatt	tccgctggaa	ctgggtgggc	acaattgcag	ctgatgacga	ctatggggcg	660
ccggggattg	agaaattccg	agagggaagct	gagggaaggg	atatctgcat	cgacttcagt	720
gaactcatct	cccagttactc	tgatgaggaa	gagatccagc	atgtggtaga	ggtgattcaa	780
aattccacgg	ccaaagtcat	cgtggttttc	tccagtggcc	cagatcttga	gccctcatc	840
aaggagattg	tccggcgcaa	tatcacgggc	aagatctggc	tggccagcga	ggcctggggc	900

agctcctccc	tgatcgccat	gcctcagtag	ttccaagtgg	ttggcggcac	cattggattc	960
gctctgaagg	ctgggcagat	cccaggcttc	cgggaattcc	tgaagaaggt	ccatcccagg	1020
aagtctgtcc	acaatggttt	tgccaaggag	ttttgggaag	aaacatttaa	ctgccacctc	1080
caagaagggtg	caaaaggacc	tttacctgtg	gacacctttc	tgagaggtca	cgaagaaagt	1140
ggcgacaggt	ttagcaacag	ctcgacagcc	ttccgacccc	tctgtacagg	ggatgagaac	1200
atcagcagtg	tcgagacccc	ttacatagat	tacacgcatt	tacggatata	ctacaatgtg	1260
tacttagcag	tctactccat	tgcccacgcc	ttgcaagata	tatataacctg	cttacctggg	1320
agagggtctct	tcaccaatgg	ctcctgtgca	gacatcaaga	aagttgaggg	gtggcaggtc	1380
ctgaagcacc	tacggcatct	aaactttaca	aacaatatgg	gggagcaggt	gacctttgat	1440
gagtgtgggtg	acctgggtggg	gaactattcc	atcatcaact	ggcacctctc	cccagaggat	1500
ggctccatcg	tgtttaagga	agtcgggtat	tacaacgtct	atgccaaaga	gggagaaaaga	1560
ctcttcatca	acgaggagaa	aatcctgtgg	agtgggttct	ccaggagggt	gcccttctcc	1620
aactgcagcc	gagactgcct	ggcaggggacc	aggaaaggga	tcattgaggg	ggagcccacc	1680
tgctgctttg	agtgtgtgga	gtgtcctgat	ggggagtata	gtgatgagac	agatgccagt	1740
gcctgtaaca	agtgtcccaga	tgacttctgg	tccaatgaga	accacacctc	ctgcttcgaa	1800
ctgccccagg	agtacatccg	ctggggcgat	gcctgggctg	tgggacctgt	caccatcgcc	1860
tgectcggtg	ccctggccac	cctgtttgtg	ctgggtgtct	ttgtgcggca	caatgccaca	1920
ccagtggtca	aggcctcagg	tcgggagctc	tgctacatcc	tgctgggtgg	tgtcttctct	1980
tgctactgca	tgaccttcat	cttcattgcc	aagccatcca	cggcagtggt	taccttacyg	2040
cgtcttggtt	tgggcactgc	cttctctgtc	tgctactcag	ccctgctcac	caagaccaac	2100
cgcattgcac	gcattctcgg	tgggggcccg	gaggggtgcc	agcggccacg	cttcatcagt	2160
cctgcctcac	aggtggccat	ctgcctggca	cttatctcgg	gpcagctgct	catcgtgggtc	2220
gcctggctgg	tggtggaggc	accgggcaca	ggcaaggaga	cagcccccca	acggcgggag	2280
gtggtgacac	tgcgctgcaa	ccaccgcgat	gcaagtatgt	tgggctcgct	ggcctacaat	2340
ttgctctcca	tgcgctctg	cacgctttat	gccttcaata	ctcgcaagtg	ccccgaaaac	2400
gtcaacgagg	ccaagttcat	tggtcttacc	atgtacacca	cctgcatcat	ctggctggca	2460
ttgttgccca	tcttctatgt	cacctccagt	gactaccggg	tacagaccac	caccatgtgc	2520
gtgtcagtc	gcctcagcgg	ctccgtgggtg	cttggtgccc	tctttgccc	caagctgcac	2580
atcatcctct	tccagccgca	gaagaacgtg	gttagccacc	gggcacccac	cagccgcttt	2640
ggcagtgctg	ctgccagggc	cagctccagc	cttgggccaag	ggtctggctc	ccagtttgtc	2700
cccactgttt	gcaatggccc	tgagggtggg	ctgtcgacaa	cgtcatcgct	tatgactctg	2760
gagtcctca	tggtgctgctg	cctgagcgag	gaggccaagg	aagcccggcg	gatcaacgac	2820
gagatcgagc	ggcagctccg	cagggacaag	cgggacgccc	gccgggagct	caagctgctg	2880
ctgctcggga	caggagagag	tggaagaggt	acgtttatca	agcagatgag	aatcatccat	2940
gggtcaggat	actctgatga	agataaaaag	ggcttcacca	agctgggtga	tcagaacatc	3000
ttcacggcca	tgacggccat	gatcagagcc	atggacacac	tcaagatccc	atacaagtat	3060
gagcacata	aggctcatgc	acaattagtt	cgagaagttg	atgtggagaa	ggtgtctgct	3120
tttgagaatc	catatgtaga	tgcaataaag	agtttatgga	atgatcctgg	aatccaggaa	3180
tgctatgata	gacgacgaga	atatcaatta	tctgactcta	ccaaatacta	tcttaatgac	3240
ttggaccgcg	tagctgaccc	tgccctacctg	cctacgcaac	aagatgtgct	tagagttcga	3300
gtccccacca	cagggatcat	cgaatacccc	tttgacttac	aaagtgtcat	tttcagaatg	3360
gtcgatgtag	ggggccaaag	gtcagagaga	agaaaatgga	tacactgctt	tgaaaatgtc	3420
acctctatca	tgtttctagt	agcgcttagt	gaatatgatc	aagttctcgt	ggagtcaaac	3480
aatgagaacc	gaatggagga	aagcaaggct	ctcttttagaa	caattatcac	ataccctcgg	3540
ttccagaact	cctcggttat	tctgttctta	aacaagaaag	atcttctaga	ggagaaaatc	3600
atgtattccc	atctagtcga	ctacttccca	gaatatgatg	gacccagag	agatgccag	3660
gcagcccag	aattcattct	gaagatgttc	gtggacctga	acccagacag	tgacaaaatt	3720
atctactccc	acttcacgtg	cgccacagac	accgagaata	tccgctttgt	ctttgctgcc	3780
gtcaaggaca	ccatcctcca	gttgaacctg	aaggactcgc	gtctgttcta	a	3831

49

<210> 33  
 <211> 1276  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Chimeric phCaR/hmGluR2\*Gqi5

<400> 33

```

Met Ala Phe Tyr Ser Cys Cys Trp Val Leu Leu Ala Leu Thr Trp His
 1              5              10              15

Thr Ser Ala Tyr Gly Pro Asp Gln Arg Ala Gln Lys Lys Gly Asp Ile
      20              25              30

Ile Leu Gly Gly Leu Phe Pro Ile His Phe Gly Val Ala Ala Lys Asp
      35              40              45

Gln Asp Leu Lys Ser Arg Pro Glu Ser Val Glu Cys Ile Arg Tyr Asn
      50              55              60

Phe Arg Gly Phe Arg Trp Leu Gln Ala Met Ile Phe Ala Ile Glu Glu
      65              70              75              80

Ile Asn Ser Ser Pro Ala Leu Leu Pro Asn Leu Thr Leu Gly Tyr Arg
      85              90              95

Ile Phe Asp Thr Cys Asn Thr Val Ser Lys Ala Leu Glu Ala Thr Leu
      100             105             110

Ser Phe Val Ala Gln Asn Lys Ile Asp Ser Leu Asn Leu Asp Glu Phe
      115             120             125

Cys Asn Cys Ser Glu His Ile Pro Ser Thr Ile Ala Val Val Gly Ala
      130             135             140

Thr Gly Ser Gly Val Ser Thr Ala Val Ala Asn Leu Leu Gly Leu Phe
      145             150             155             160

Tyr Ile Pro Gln Val Ser Tyr Ala Ser Ser Ser Arg Leu Leu Ser Asn
      165             170             175

Lys Asn Gln Phe Lys Ser Phe Leu Arg Thr Ile Pro Asn Asp Glu His
      180             185             190

Gln Ala Thr Ala Met Ala Asp Ile Ile Glu Tyr Phe Arg Trp Asn Trp
      195             200             205

Val Gly Thr Ile Ala Ala Asp Asp Asp Tyr Gly Arg Pro Gly Ile Glu
      210             215             220

Lys Phe Arg Glu Glu Ala Glu Glu Arg Asp Ile Cys Ile Asp Phe Ser
      225             230             235             240

```



50

Glu Leu Ile Ser Gln Tyr Ser Asp Glu Glu Glu Ile Gln His Val Val  
 245 250 255  
 Glu Val Ile Gln Asn Ser Thr Ala Lys Val Ile Val Val Phe Ser Ser  
 260 265 270  
 Gly Pro Asp Leu Glu Pro Leu Ile Lys Glu Ile Val Arg Arg Asn Ile  
 275 280 285  
 Thr Gly Lys Ile Trp Leu Ala Ser Glu Ala Trp Ala Ser Ser Ser Leu  
 290 295 300  
 Ile Ala Met Pro Gln Tyr Phe His Val Val Gly Gly Thr Ile Gly Phe  
 305 310 315 320  
 Ala Leu Lys Ala Gly Gln Ile Pro Gly Phe Arg Glu Phe Leu Lys Lys  
 325 330 335  
 Val His Pro Arg Lys Ser Val His Asn Gly Phe Ala Lys Glu Phe Trp  
 340 345 350  
 Glu Glu Thr Phe Asn Cys His Leu Gln Glu Gly Ala Lys Gly Pro Leu  
 355 360 365  
 Pro Val Asp Thr Phe Leu Arg Gly His Glu Glu Ser Gly Asp Arg Phe  
 370 375 380  
 Ser Asn Ser Ser Thr Ala Phe Arg Pro Leu Cys Thr Gly Asp Glu Asn  
 385 390 395 400  
 Ile Ser Ser Val Glu Thr Pro Tyr Ile Asp Tyr Thr His Leu Arg Ile  
 405 410 415  
 Ser Tyr Asn Val Tyr Leu Ala Val Tyr Ser Ile Ala His Ala Leu Gln  
 420 425 430  
 Asp Ile Tyr Thr Cys Leu Pro Gly Arg Gly Leu Phe Thr Asn Gly Ser  
 435 440 445  
 Cys Ala Asp Ile Lys Lys Val Glu Ala Trp Gln Val Leu Lys His Leu  
 450 455 460  
 Arg His Leu Asn Phe Thr Asn Asn Met Gly Glu Gln Val Thr Phe Asp  
 465 470 475 480  
 Glu Cys Gly Asp Leu Val Gly Asn Tyr Ser Ile Ile Asn Trp His Leu  
 485 490 495  
 Ser Pro Glu Asp Gly Ser Ile Val Phe Lys Glu Val Gly Tyr Tyr Asn  
 500 505 510  
 Val Tyr Ala Lys Lys Gly Glu Arg Leu Phe Ile Asn Glu Glu Lys Ile  
 515 520 525

51

Leu Trp Ser Gly Phe Ser Arg Glu Val Pro Phe Ser Asn Cys Ser Arg  
 530 535 540  
 Asp Cys Leu Ala Gly Thr Arg Lys Gly Ile Ile Glu Gly Glu Pro Thr  
 545 550 555 560  
 Cys Cys Phe Glu Cys Val Glu Cys Pro Asp Gly Glu Tyr Ser Asp Glu  
 565 570 575  
 Thr Asp Ala Ser Ala Cys Asn Lys Cys Pro Asp Asp Phe Trp Ser Asn  
 580 585 590  
 Glu Asn His Thr Ser Cys Phe Glu Leu Pro Gln Glu Tyr Ile Arg Trp  
 595 600 605  
 Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys Leu Gly Ala  
 610 615 620  
 Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His Asn Ala Thr  
 625 630 635 640  
 Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile Leu Leu Gly  
 645 650 655  
 Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile Ala Lys Pro  
 660 665 670  
 Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly Thr Ala Phe  
 675 680 685  
 Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg Ile Ala Arg  
 690 695 700  
 Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg Phe Ile Ser  
 705 710 715 720  
 Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser Gly Gln Leu  
 725 730 735  
 Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly Thr Gly Lys  
 740 745 750  
 Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg Cys Asn His  
 755 760 765  
 Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val Leu Leu Ile  
 770 775 780  
 Ala Leu Cys Thr Leu Tyr Ala Phe Asn Thr Arg Lys Cys Pro Glu Asn  
 785 790 795 800  
 Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr Thr Cys Ile  
 805 810 815

Ile Trp Leu Ala Leu Leu Pro Ile Phe Tyr Val Thr Ser Ser Asp Tyr  
 820 825 830  
 Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu Ser Gly Ser  
 835 840 845  
 Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile Ile Leu Phe  
 850 855 860  
 Gln Pro Gln Lys Asn Val Ser His Arg Ala Pro Thr Ser Arg Phe  
 865 870 875 880  
 Gly Ser Ala Ala Ala Arg Ala Ser Ser Ser Leu Gly Gln Gly Ser Gly  
 885 890 895  
 Ser Gln Phe Val Pro Thr Val Cys Asn Gly Arg Glu Val Val Asp Ser  
 900 905 910  
 Thr Thr Ser Ser Leu Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu  
 915 920 925  
 Ser Glu Glu Ala Lys Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg  
 930 935 940  
 Gln Leu Arg Arg Asp Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu  
 945 950 955 960  
 Leu Leu Gly Thr Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met  
 965 970 975  
 Arg Ile Ile His Gly Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe  
 980 985 990  
 Thr Lys Leu Val Tyr Gln Asn Ile Phe Thr Ala Met Gln Ala Met Ile  
 995 1000 1005  
 Arg Ala Met Asp Thr Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys  
 1010 1015 1020  
 Ala His Ala Gln Leu Val Arg Glu Val Asp Val Glu Lys Val Ser Ala  
 1025 1030 1035 1040  
 Phe Glu Asn Pro Tyr Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro  
 1045 1050 1055  
 Gly Ile Gln Glu Cys Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp  
 1060 1065 1070  
 Ser Thr Lys Tyr Tyr Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala  
 1075 1080 1085  
 Tyr Leu Pro Thr Gln Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr  
 1090 1095 1100

53

Gly Ile Ile Glu Tyr Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met  
 1105 1110 1115 1120  
 Val Asp Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys  
 1125 1130 1135  
 Phe Glu Asn Val Thr Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr  
 1140 1145 1150  
 Asp Gln Val Leu Val Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser  
 1155 1160 1165  
 Lys Ala Leu Phe Arg Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser  
 1170 1175 1180  
 Ser Val Ile Leu Phe Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile  
 1185 1190 1195 1200  
 Met Tyr Ser His Leu Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln  
 1205 1210 1215  
 Arg Asp Ala Gln Ala Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp  
 1220 1225 1230  
 Leu Asn Pro Asp Ser Asp Lys Ile Ile Tyr Ser His Phe Thr Cys Ala  
 1235 1240 1245  
 Thr Asp Thr Glu Asn Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr  
 1250 1255 1260  
 Ile Leu Gln Leu Asn Leu Lys Asp Cys Gly Leu Phe  
 1265 1270 1275

<210> 34  
 <211> 3105  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Chimeric hmGluR2/hCaR

<400> 34

atgggatcgc	tgcttgcgct	cccggcactg	ctgctgctgt	ggggtgctgt	ggctgagggc	60
ccagccaaga	aggtgctgac	cctggaggga	gacttggtgc	tgggtgggct	gttcccagtg	120
caccagaagg	gcggcccagc	agaggactgt	ggctctgtca	atgagcaccg	tggcatccag	180
cgcttgagg	ccatgctttt	tgcactggac	cgcatcaacc	gtgaccgcga	cctgctgcct	240
ggcgtgcgcc	tgggtgcaca	catcctcgac	agttgctcca	aggacacaca	tgcgctggag	300
caggcactgg	actttgtgcg	tgccctcactc	agccgtgggtg	ctgatggctc	acgccacatc	360
tgccccgacg	gctcttatgc	gacccatggt	gatgctccca	ctgccatcac	tggtgttatt	420
ggcggttcct	acagtgatgt	ctccatccag	gtggccaacc	tcttgaggct	atttcagatc	480
ccacagatta	gctacgcctc	taccagtgcc	aaagtgagtg	acaagtcccg	ctatgactac	540

tttgcccgcga	cagtgcctcc	tgacttcttc	caagccaagg	ccatggctga	gattctccgc	600
ttcttcaact	ggacctatgt	gtccactgtg	gcgtctgagg	gcgactatgg	cgagacaggc	660
attgaggect	ttgagctaga	ggctcgtgcc	cgcaacatct	gtgtggccac	ctcggagaaa	720
gtgggccgtg	ccatgagccg	cgcggccttt	gaggggtgtg	tgcgagccct	gctgcagaa	780
cccagtgccc	gcgtggctgt	cctgttcacc	cgttctgagg	atgcccggga	gctgcttgct	840
gccagccagc	gcctcaatgc	cagcttcacc	tgggtggcca	gtgatggtg	gggggcccctg	900
gagagtgtgg	tggcaggcag	tgagggggct	gctgaggtg	ctatcaccat	cgagctggcc	960
tcctacccca	tcagtgaatt	tgccctctac	ttccagagcc	tggacccttg	gaacaacagc	1020
cggaacccct	ggttccgtga	attctgggag	cagagggttc	gctgcagctt	ccggcagcga	1080
gactgcgcag	cccactctct	ccgggctgtg	ccctttgagc	aggagtccaa	gatcatgttt	1140
gtggtcaatg	cagtgtacgc	catggcccat	gcgctccaca	acatgcaccg	tgccctctgc	1200
cccaacacca	cccggctctg	tgacgcgatg	cggccagtta	acgggcgcgg	cctctacaag	1260
gactttgtgc	tcaacgtcaa	gtttgatgcc	ccctttcgcc	cagctgacac	ccacaatgag	1320
gtccgctttg	accgctttgg	tgatggtatt	ggccgctaca	acatcttcac	ctatctgcgt	1380
gcaggcagtg	ggcgctatcg	ctaccagaag	gtgggctact	gggcagaagg	cttgactctg	1440
gacaccagcc	tcatcccatg	ggcctcacc	tcagccggcc	ccctgcccgc	ctctcgctgc	1500
agttagccct	gcctccagaa	tgaggtgaag	agtgtgcagc	cgggcgaagt	ctgctgctgg	1560
ctctgcattc	cgtgccagcc	ctatgagtac	cgattggacg	aattcacttg	cgctgattgt	1620
ggcctggggc	actggcccaa	tgccagcctg	actggctgct	tcgaactgcc	ccaggagtac	1680
atccgctggg	gcgatgcctg	ggctgtggga	cctgtcacca	tcgcctgcct	cggtgccttg	1740
gccaccctct	ttgtgctggg	tgtctttgtg	cggcacaatg	ccacaccagt	ggtcaaggcc	1800
tcaggtcggg	agctctgcta	catcctgctg	ggtggtgtct	tcctctgcta	ctgcatgacc	1860
ttcatcttca	ttgccaaagg	atccacggca	gtgtgtacct	tacggcgtct	tggtttgggc	1920
actgccttct	ctgtctgcta	ctcagccctg	ctcaccaaga	ccaaccgcat	tgcacgcata	1980
ttcgggtggg	cccgggaggg	tgccagcgg	ccacgcttca	tcagtcctgc	ctcacagggtg	2040
gccatcttgc	tggcacttat	ctcggggccag	ctgcctcatg	tggtcgcctg	gctggtggtg	2100
gaggcacccg	gcacaggcaa	ggagacagcc	cccgaacggc	gggaggtggt	gacactgcgc	2160
tgcaaccacc	gcgatgcaag	tatgttgggc	tcgctggcct	acaatgtgct	cctcatcgcg	2220
ctctgcacgc	tttatgcctt	caagactcgc	aagtgcgccg	aaaacttcaa	cgaggccaag	2280
ttcattggct	tcaccatgta	caccacctgc	atcatctggc	tggcattcct	gcccattctt	2340
tatgtcacct	ccagtgaact	ccgggtacag	accaccacca	tgtgcgtgtc	agtcagcctc	2400
agcggctccg	tgggtgcttg	ctgcctcttt	gcgcccgaag	tgcacatcat	cctcttccag	2460
ccgcagaaga	acaccatcga	ggaggtgcgt	tgcagcaccg	cagctcacgc	tttcaagggtg	2520
gctgccgggg	ccacgctgcg	ccgcagcaac	gtctcccgc	agcgggtccg	cagccttgga	2580
ggctccacgg	gatccacccc	ctcctcctcc	atcagcagca	agagcaacag	cgaagacca	2640
ttcccacagc	ccgagaggca	gaagcagcag	cagccgctgg	ccctaaccga	gcaagagcag	2700
cagcagcagc	ccctgaccct	cccacagcag	caacgatctc	agcagcagcc	cagatgcaag	2760
cagaagggtca	tctttggcag	cggcacggtc	accttctcac	tgagctttga	tgagcctcag	2820
aagaacgcca	tggcccacgg	gaattctacg	caccagaact	ccctggaggc	ccagaaaagc	2880
agcgatacgc	tgacccgaca	ccagccatta	ctcccgtctg	agtgcgggga	aaeggactta	2940
gatctgaccg	tccaggaaac	aggtctgcaa	ggacctgtgg	gtggagacca	gcggccagag	3000
gtggaggacc	ctgaagagtt	gtccccagca	cttgtagtgt	ccagttcaca	gagctttgtc	3060
atcagtggtg	gaggcagcac	tgttacagaa	aacgtagtga	attca		3105

&lt;210&gt; 35

&lt;211&gt; 1035

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Chimeric hmGluR2/hCaR

55

&lt;400&gt; 35

Met Gly Ser Leu Leu Ala Leu Pro Ala Leu Leu Leu Leu Trp Gly Ala  
 1 5 10 15  
 Val Ala Glu Gly Pro Ala Lys Lys Val Leu Thr Leu Glu Gly Asp Leu  
 20 25 30  
 Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu  
 35 40 45  
 Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala  
 50 55 60  
 Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro  
 65 70 75 80  
 Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr  
 85 90 95  
 His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg  
 100 105 110  
 Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr  
 115 120 125  
 His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr  
 130 135 140  
 Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile  
 145 150 155 160  
 Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser  
 165 170 175  
 Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala  
 180 185 190  
 Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser  
 195 200 205  
 Thr Val Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe  
 210 215 220  
 Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys  
 225 230 235 240  
 Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala  
 245 250 255  
 Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser  
 260 265 270

56

Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser  
 275 280 285  
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val  
 290 295 300  
 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala  
 305 310 315 320  
 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro  
 325 330 335  
 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg  
 340 345 350  
 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg  
 355 360 365  
 Ala Val Pro Phe Glu Gln Glu Ser Lys Ile Met Phe Val Val Asn Ala  
 370 375 380  
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys  
 385 390 395 400  
 Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg  
 405 410 415  
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe  
 420 425 430  
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp  
 435 440 445  
 Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly  
 450 455 460  
 Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu  
 465 470 475 480  
 Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Pro  
 485 490 495  
 Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val  
 500 505 510  
 Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr  
 515 520 525  
 Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr  
 530 535 540  
 Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr  
 545 550 555 560

57

Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys  
 565 570 575  
 Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His  
 580 585 590  
 Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile  
 595 600 605  
 Leu Leu Gly Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile  
 610 615 620  
 Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly  
 625 630 635 640  
 Thr Ala Phe Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg  
 645 650 655  
 Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg  
 660 665 670  
 Phe Ile Ser Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser  
 675 680 685  
 Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly  
 690 695 700  
 Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg  
 705 710 715 720  
 Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val  
 725 730 735  
 Leu Leu Ile Ala Leu Cys Thr Leu Tyr Ala Phe Lys Thr Arg Lys Cys  
 740 745 750  
 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr  
 755 760 765  
 Thr Cys Ile Ile Trp Leu Ala Phe Leu Pro Ile Phe Tyr Val Thr Ser  
 770 775 780  
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu  
 785 790 795 800  
 Ser Gly Ser Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile  
 805 810 815  
 Ile Leu Phe Gln Pro Gln Lys Asn Thr Ile Glu Glu Val Arg Cys Ser  
 820 825 830  
 Thr Ala Ala His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg  
 835 840 845



58

Ser Asn Val Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly  
 850 855 860  
 Ser Thr Pro Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro  
 865 870 875 880  
 Phe Pro Gln Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr  
 885 890 895  
 Gln Gln Glu Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg  
 900 905 910  
 Ser Gln Gln Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly  
 915 920 925  
 Thr Val Thr Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met  
 930 935 940  
 Ala His Gly Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser  
 945 950 955 960  
 Ser Asp Thr Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly  
 965 970 975  
 Glu Thr Asp Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro  
 980 985 990  
 Val Gly Gly Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser  
 995 1000 1005  
 Pro Ala Leu Val Val Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly  
 1010 1015 1020  
 Gly Ser Thr Val Thr Glu Asn Val Val Asn Ser  
 1025 1030 1035

&lt;210&gt; 36

&lt;211&gt; 4185

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Chimeric pmGluR2//CaR\*Gα<sub>i</sub>5

&lt;400&gt; 36

atgggatcgc	tgcttgcgct	cccggcactg	ctgctgctgt	ggggtgctgt	ggctgagggc	60
ccagccaaga	aggtgctgac	cctggaggga	gacttggtgc	tgggtgggct	gttcccagtg	120
caccagaagg	gcggcccagc	agaggactgt	ggtcctgtca	atgagcaccg	tggcatccag	180
cgcctggagg	ccatgctttt	tgactgggac	cgcacccaac	gtgacccgca	cctgctgcct	240
ggcgtgcgcc	tgggtgcaca	catectcgac	agttgtccca	aggacacaca	tgcgctggag	300
caggcactgg	actttgtgog	tgctcactc	agccgtgggtg	ctgatggctc	acgccacatc	360

tgccccgacg	gctcttatgc	gacccatggt	gatgctccca	ctgccatcac	tggtgttatt	420
ggcgggttcct	acagtgatgt	ctccatccag	gtggccaacc	tcttgaggct	atttcagatc	480
ccacagatta	gctacgcctc	taccagtgcc	aagctgagtg	acaagtcccg	ctatgactac	540
tttgcccgca	cagtgcctcc	tgacttcttc	caagccaagg	ccatggctga	gattctccgc	600
ttcttcaact	ggacctatgt	gtccactgtg	gcgtctgagg	gcgactatgg	cgagacaggc	660
attgaggcct	ttgagctaga	ggctcgtgcc	cgcaacatct	gtgtggccac	ctcggagaaa	720
gtgggcccgtg	ccatgagccg	cgcggccttt	gaggggtgtg	tgcgagccct	gctgcagaag	780
cccagtgcce	gcgtggctgt	cctgttcacc	cgttctgagg	atgcccggga	gctgcttgct	840
gccagccagc	gcctcaatgc	cagcttcacc	tggttgccca	gtgatggtg	gggggcccctg	900
gagagtgtgg	tgccaggcag	tgagggggct	gctgaggggtg	ctatcaccat	cgagctggcc	960
tcctacccca	tcagtgactt	tgccctctac	ttccagagcc	tggaaccttg	gaacaacagc	1020
cggaacccct	ggttccgtga	attctggggag	cagaggttcc	gctgcagctt	ccggcagcga	1080
gactgcgcag	cccactctct	ccgggctgtg	ccctttgagc	aggagtccaa	gatcatgttt	1140
gtggtcaatg	cagtgtacgc	catggcccat	gcgctccaca	acatgcaccg	tgccctctgc	1200
cccaacacca	cccggtctctg	tgacgcgatg	cggccagtta	acgggcgcgc	cctctacaag	1260
gactttgtgc	tcaacgtcaa	gtttgatgcc	ccctttcgcc	cagctgacac	ccacaatgag	1320
gtccgctttg	accgcttttg	tgatggtatt	ggccgctaca	acatcttcac	ctatctgcgt	1380
gcaggcagtg	ggcgtatctg	ctaccagaag	gtgggctact	gggcagaagg	cttgactctg	1440
gacaccagcc	tcaccccatg	ggcctcaccc	tcagccggcc	ccctgcccgc	ctctcgctgc	1500
agtgagccct	gcctccagaa	tgaggtgaag	agtgtgcagc	cgggcgaagt	ctgctgctgg	1560
ctctgcattc	cgtgccagcc	ctatgagtac	cgattggacg	aattcacttg	cgctgattgt	1620
ggcctgggct	actggcccaa	tgccagcctg	actggctgct	tcgaactgcc	ccaggagtac	1680
atccgctggg	gcgatgcctg	ggctgtggga	cctgtcacca	tcgcctgcct	cggtgccctg	1740
gccaccctct	ttgtgctggg	tgtctttgtg	cggcacaatg	ccacaccagt	ggtcaaggcc	1800
tcaggctcggg	agctctgcta	cactctgctg	ggtggtgtct	tcctctgcta	ctgcatgacc	1860
ttcatcttca	ttgccaagcc	atccacggca	gtgtgtacct	tacggcgtct	tggtttgggc	1920
actgccttct	ctgtctgcta	ctcagccctg	ctcaccaaga	ccaaccgcat	tgacgcgcatc	1980
ttcgggtggg	cccgggagg	tgcccagcgg	ccacgcttca	tcagtcctgc	ctcacagggtg	2040
gcatctgcc	tgccacttat	ctcgggccag	ctgctcatcg	tggtcgccctg	gctggtgggtg	2100
gaggcaccgg	gcacaggcaa	ggagacagcc	cccgaaccgc	gggaggtggt	gacactgcgc	2160
tgcaaccacc	gcgatgcaag	tatgttgggc	tcgctggcct	acaatgtgct	cctcatcgcg	2220
ctctgcacgc	tttatgcctt	caagactcgc	aagtgcctcg	aaaacttcaa	cgaggccaag	2280
ttcatgtggt	tcaccatgta	caccacctgc	atcatctggc	tggtattcct	gcccattcttc	2340
tatgtcacct	ccagtgacta	ccgggtacag	accaccacca	tgtgcgtgtc	agtcagcctc	2400
agcggtcccg	tggtgcttgg	ctgcctcttt	gcgccaagc	tgacatcat	cctcttcag	2460
ccgcagaaga	acaccatcga	ggaggtgcgt	tgacgacccg	cagctcacgc	tttcaagggtg	2520
gctgcocggg	ccacgctgcg	ccgcagcaac	gtctcccgca	agcggctccag	cagccttgga	2580
ggctccacgg	gatccacccc	ctcctcctcc	atcagcagca	agagcaacag	cgaagaccca	2640
ttccacagc	ccgagaggca	gaagcagcag	cagccgctgg	ccctaaccga	gcaagagcag	2700
cagcagcagc	ccctgaccct	cccacagcag	caacgatctc	agcagcagcc	cagatgcaag	2760
cagaaggcca	tctttggcag	cggcacggtc	accttctcac	tgagctttga	tgagcctcag	2820
aagaacgcca	tgccccacgg	gaattctacg	caccagaact	ccctggaggc	ccagaaaagc	2880
agcgatacgc	tgacccgaca	ccagccatta	ctcccgtgct	agtgcgggga	aacggactta	2940
gatctgaccg	tccaggaaac	aggtctgcga	ggacctgtgg	gtggagacca	gcggccagag	3000
gtggaggacc	ctgaagagtt	gtccccagca	cttgtagtgt	ccagttcaca	gagctttgtc	3060
atcagtgggtg	gaggcagcac	tgttacagaa	aacgtagtga	attcaatgac	tctggagtcc	3120
atcatggcgt	gctgcctgag	cgaggaggcc	aagggaagccc	ggcggatcaa	cgacgagatc	3180
gagcggcagc	tccgcaggga	caagcgggac	gcccgcgggg	agctcaagct	gctgctgctc	3240
gggacaggag	agagtggcaa	gagtacgttt	atcaagcaga	tgagaatcat	ccatgggtca	3300
ggatactctg	atgaagataa	aaggggcttc	accaaagctgg	tgtatcagaa	catcttcacg	3360
gcatatgcag	ccatgatcag	agccatggac	acactcaaga	tcccatataa	gtatgagcac	3420
aataaggctc	atgcacaatt	agttcgagaa	gttgatgtgg	agaagggtgc	tgcttttgag	3480
aatccatatg	tagatgcaat	aaagagttaa	tggaatgata	ctggaatcca	ggaatgctat	3540
gatagacgac	gagaatatca	attatctgac	tctaccaaata	actatcttaa	tgacttggac	3600
cgcgtagctg	accctgccta	cctgcctacg	caacaagatg	tgcttagagt	tcgagtcccc	3660

```

accacagggg tcatcgaata cccctttgac ttacaaagtg tcattttcag aatggtcgat 3720
gtagggggcc aaaggtcaga gagaagaaaa tggatacact gctttgaaaa tgtcacctct 3780
atcatgtttc tagtagcgct tagtgaatat gatcaagttc tcgtggagtc agacaatgag 3840
aaccgaatgg aggaaagcaa ggctctcttt agaacaatta tcacataccc ctggttccag 3900
aactcctcgg ttattctgtt cttaacaag aaagatcttc tagaggagaa aatcatgtat 3960
tcccatctag tcgactactt cccagaatat gatggacccc agagagatgc ccaggcagcc 4020
cgagaattca ttctgaagat gttcgtggac ctgaacccag acagtgacaa aattatctac 4080
tcccacttca cgtgcgccac agacaccgag aatatccgct ttgtctttgc tgccgtcaag 4140
gacaccatcc tccagttgaa cctgaaggac tgcggtctgt tctaa 4185

```

&lt;210&gt; 37

&lt;211&gt; 1394

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Chimeric pmGluR2//CaR\*G $\alpha$ <sub>i5</sub>

&lt;400&gt; 37

```

Met Gly Ser Leu Leu Ala Leu Pro Ala Leu Leu Leu Leu Trp Gly Ala
 1              5              10              15

Val Ala Glu Gly Pro Ala Lys Lys Val Leu Thr Leu Glu Gly Asp Leu
20              25              30

Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu
35              40              45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
50              55              60

Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
65              70              75              80

Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
85              90              95

His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
100             105             110

Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr
115             120             125

His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr
130             135             140

Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile
145             150             155             160

```

61

Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser  
 165 170 175  
 Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala  
 180 185 190  
 Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser  
 195 200 205  
 Thr Val Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe  
 210 215 220  
 Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys  
 225 230 235 240  
 Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala  
 245 250 255  
 Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser  
 260 265 270  
 Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser  
 275 280 285  
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val  
 290 295 300  
 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala  
 305 310 315 320  
 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro  
 325 330 335  
 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg  
 340 345 350  
 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg  
 355 360 365  
 Ala Val Pro Phe Glu Gln Glu Ser Lys Ile Met Phe Val Val Asn Ala  
 370 375 380  
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys  
 385 390 395 400  
 Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg  
 405 410 415  
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe  
 420 425 430  
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp  
 435 440 445

62

Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly  
 450 455 460

Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu  
 465 470 475 480

Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Pro  
 485 490 495

Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val  
 500 505 510

Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr  
 515 520 525

Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr  
 530 535 540

Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr  
 545 550 555 560

Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys  
 565 570 575

Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His  
 580 585 590

Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile  
 595 600 605

Leu Leu Gly Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile  
 610 615 620

Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly  
 625 630 635 640

Thr Ala Phe Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg  
 645 650 655

Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg  
 660 665 670

Phe Ile Ser Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser  
 675 680 685

Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly  
 690 695 700

Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg  
 705 710 715 720

Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val  
 725 730 735

63

Leu Leu Ile Ala Leu Cys Thr Leu Tyr Ala Phe Lys Thr Arg Lys Cys  
 740 745 750  
 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr  
 755 760 765  
 Thr Cys Ile Ile Trp Leu Ala Phe Leu Pro Ile Phe Tyr Val Thr Ser  
 770 775 780  
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu  
 785 790 795 800  
 Ser Gly Ser Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile  
 805 810 815  
 Ile Leu Phe Gln Pro Gln Lys Asn Thr Ile Glu Glu Val Arg Cys Ser  
 820 825 830  
 Thr Ala Ala His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg  
 835 840 845  
 Ser Asn Val Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly  
 850 855 860  
 Ser Thr Pro Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro  
 865 870 875 880  
 Phe Pro Gln Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr  
 885 890 895  
 Gln Gln Glu Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg  
 900 905 910  
 Ser Gln Gln Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly  
 915 920 925  
 Thr Val Thr Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met  
 930 935 940  
 Ala His Gly Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser  
 945 950 955 960  
 Ser Asp Thr Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly  
 965 970 975  
 Glu Thr Asp Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro  
 980 985 990  
 Val Gly Gly Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser  
 995 1000 1005  
 Pro Ala Leu Val Val Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly  
 1010 1015 1020

Gly Ser Thr Val Thr Glu Asn Val Val Asn Ser Met Thr Leu Glu Ser  
 1025 1030 1035 1040  
 Ile Met Ala Cys Cys Leu Ser Glu Glu Ala Lys Glu Ala Arg Arg Ile  
 1045 1050 1055  
 Asn Asp Glu Ile Glu Arg Gln Leu Arg Arg Asp Lys Arg Asp Ala Arg  
 1060 1065 1070  
 Arg Glu Leu Lys Leu Leu Leu Leu Gly Thr Gly Glu Ser Gly Lys Ser  
 1075 1080 1085  
 Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly Ser Gly Tyr Ser Asp  
 1090 1095 1100  
 Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr Gln Asn Ile Phe Thr  
 1105 1110 1115 1120  
 Ala Met Gln Ala Met Ile Arg Ala Met Asp Thr Leu Lys Ile Pro Tyr  
 1125 1130 1135  
 Lys Tyr Glu His Asn Lys Ala His Ala Gln Leu Val Arg Glu Val Asp  
 1140 1145 1150  
 Val Glu Lys Val Ser Ala Phe Glu Asn Pro Tyr Val Asp Ala Ile Lys  
 1155 1160 1165  
 Ser Leu Trp Asn Asp Pro Gly Ile Gln Glu Cys Tyr Asp Arg Arg Arg  
 1170 1175 1180  
 Glu Tyr Gln Leu Ser Asp Ser Thr Lys Tyr Tyr Leu Asn Asp Leu Asp  
 1185 1190 1195 1200  
 Arg Val Ala Asp Pro Ala Tyr Leu Pro Thr Gln Gln Asp Val Leu Arg  
 1205 1210 1215  
 Val Arg Val Pro Thr Thr Gly Ile Ile Glu Tyr Pro Phe Asp Leu Gln  
 1220 1225 1230  
 Ser Val Ile Phe Arg Met Val Asp Val Gly Gly Gln Arg Ser Glu Arg  
 1235 1240 1245  
 Arg Lys Trp Ile His Cys Phe Glu Asn Val Thr Ser Ile Met Phe Leu  
 1250 1255 1260  
 Val Ala Leu Ser Glu Tyr Asp Gln Val Leu Val Glu Ser Asp Asn Glu  
 1265 1270 1275 1280  
 Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg Thr Ile Ile Thr Tyr  
 1285 1290 1295  
 Pro Trp Phe Gln Asn Ser Ser Val Ile Leu Phe Leu Asn Lys Lys Asp  
 1300 1305 1310

Leu Leu Glu Glu Lys Ile Met Tyr Ser His Leu Val Asp Tyr Phe Pro  
 1315 1320 1325  
 Glu Tyr Asp Gly Pro Gln Arg Asp Ala Gln Ala Ala Arg Glu Phe Ile  
 1330 1335 1340  
 Leu Lys Met Phe Val Asp Leu Asn Pro Asp Ser Asp Lys Ile Ile Tyr  
 1345 1350 1355 1360  
 Ser His Phe Thr Cys Ala Thr Asp Thr Glu Asn Ile Arg Phe Val Phe  
 1365 1370 1375  
 Ala Ala Val Lys Asp Thr Ile Leu Gln Leu Asn Leu Lys Asp Cys Gly  
 1380 1385 1390  
 Leu Phe

<210> 38  
 <211> 3177  
 <212> DNA  
 <213> Artificial Sequence  
  
 <220>  
 <223> Chimeric hmGluR8/hCaR

<400> 38

atggtatg	cg	agggaa	agcg	atcagc	ctct	tgccct	tggt	tctt	ctct	ctt	gaccg	ccaag	60
ttctact	gga	tcctca	caaat	gatgca	aaaga	actcac	agcc	aggagt	atgc	ccattc	ccata		120
ggggtg	gatg	gggac	attat	tttggg	gggt	ctctt	ccctg	tccacg	caaa	gggag	agaga		180
ggggtg	ccct	gtggg	gagct	gaaga	aagg	aa	ggg	gatc	acag	actg	gga	ggccat	240
tatgca	attg	accag	attaa	caagg	accct	gatct	ccctt	ccaac	atcac	tctg	gggtg	ctc	300
cgcatc	ctcg	acacgt	gctc	taggg	acacc	tatg	ctttg	agcag	tctct	aacatt	cg	tg	360
caggca	ttaa	tagaga	aaaga	tgctt	cggat	gtga	agtgtg	cta	atgg	gaga	tccacc	att	420
ttcac	caagc	ccgaca	agat	ttctg	gcgtc	atagg	tgtg	cagca	agctc	cgtg	tccatc		480
atggtt	gcta	acattt	taag	actttt	taag	atac	ctcaa	tcag	ctatgc	atcc	acagcc		540
ccagag	ctaa	gtgata	aacac	cagg	atgac	ttttt	ctctc	gagt	gggtcc	gcct	gactcc		600
tacca	agccc	aagcc	atggt	ggac	atcgtg	acag	cactgg	gatg	gaatta	tg	tttcg	aca	660
ctggc	ttctg	agggg	aaacta	tggtg	agagc	ggtg	tggagg	cctt	caccca	gatc	tcgagg		720
gagatt	gggtg	gtgtt	tgc	at	cagtc	ca	gaaa	atcc	cag	tgaacc	aagac	ctgga	780
gaattt	gaaa	aaatt	atcaa	acgc	ctgcta	gaa	acaccta	atg	ctcg	agc	agt	gattatg	840
tttg	ccaatg	aggat	gacat	cagg	aggata	ttg	gaagc	ag	caaaaa	aa	accaa	agt	900
gggc	attt	ct	tggtt	g	ctcag	atagt	tggg	gatcca	aa	atag	cacc	tgtctatcag	960
caag	aggaga	ttgc	agaagg	ggct	gtgaca	at	tttg	ccca	aac	gagcatc	aatt	gatgga	1020
tttg	atcgat	acttt	tagaag	ccga	actctt	gcc	aataatc	ga	agaa	atgt	gtggtt	tgca	1080
gaatt	ctggg	aggaga	aattt	tgg	ctgcaag	ttag	gatcac	atgg	gaaa	ag	gaacag	tcat	1140
ataa	agaaat	gcac	agggct	ggag	cgaatt	gctc	gggatt	cat	cttatga	acag	gaagga		1200
aag	gtccaat	ttg	taattga	tgct	gtatat	tcc	atggctt	acg	ccctgca	caat	atgcac		1260
aaag	atctct	gc	ctggata	catt	ggcctt	tgt	ccacgaa	tg	ag	taccat	tgat	gggaaa	1320
gag	ctacttg	gtt	atattcg	ggct	gtaaa	ttta	atggca	gtg	ctggc	ac	tcct	gtcact	1380
ttta	atgaaa	acg	gagatgc	tcct	ggacgt	tat	gatatct	tcc	agtatca	aata	accaac		1440
aaa	agcacag	agt	acaaagt	cat	cggccac	tgg	accaatc	ag	cttcatct	aaa	agt	ggaa	1500



```

gacatgcagt gggctcatag agaacatact caccggcggt ctgtctgcag cctgcccgtgt 1560
aagccagggg agaggaagaa aacggtgaaa ggggtccctt gctgctggca ctgtgaacgc 1620
tgtgaagggt acaactacca ggtggatgag ctgtcctgtg aactttgccc tctggatcag 1680
agacccaaca tgaaccgcac aggtgccag cttatcccca tcatcaaatt ggagtggcat 1740
tctccctggg ctgtgggtgc tgtgtttgtt gcaatattgg gaatcatcgc caccaccttt 1800
gtgatcgtga cctttgtccg ctataatgac acacctatcg tgagggcttc aggacgcgaa 1860
cttagttacg tgctcctaac ggggattttt ctctgttatt caatcacgtt tttaatgatt 1920
gcagcaccag atacaatcat atgctccttc cgacgggtct tcctaggact tggcatgtgt 1980
ttcagctatg cagcccttct gaccaaaca aaccgtatcc accgaatatt tgagcagggg 2040
aagaaatctg tcacagcgcc caagttcatt agtccagcat ctcagctggt gatcaccttc 2100
agcctcatct ccgtccagct ccttgagtg tttgtctggt ttgttggtga tccccccac 2160
atcatcattg actatggaga gcagcggaca ctatagccag agaaggccag gggagtgtct 2220
aagtgtgaca tttctgatct ctactcatt tgttcacttg gatacagtat cctcttgatg 2280
gtcacttgta ctgtttatgc cattaacacg agaggtgtcc cagagacttt caatgaagcc 2340
aaacctattg gatttaccat gtataccacc tgcattcatt ggtagcttt catccccatc 2400
ttttttgta cagcccagtc agcagaaaag atgtacatcc agacaacaac acttactgtc 2460
tccatgagtt taagtgtctc agtatctctg ggcattgctc atatgcccac gggttatatt 2520
ataatttttc atccagaaca gaataccatc gaggaggtgc gttgcagcac cgcagctcac 2580
gctttcaagg tggtgcccgc ggccacgctg cgccgcagca acgtctcccg caagcgggcc 2640
agcagccttg gaggtccac gggatccacc ccctcctcct ccatcagcag caagagcaac 2700
agcgaagacc cattcccaca gcccagagag cagaagcagc agcagccgct ggccctaacc 2760
cagcaagagc agcagcagca gcccctgacc ctcccacagc agcaacgatc tcagcagcag 2820
cccagatgca agcagaaggt catctttggc agcggcacgg tcaccttctc actgagcttt 2880
gatgagcctc agaagaacgc catggcccac ggggaattcta cgcaccagaa ctccctggag 2940
gcccagaaaa gcagcgatac gctgaccgga caccagccat tactcccgtc gcagtgcggg 3000
gaaacggact tagatctgac cgtccaggaa acaggtctgc aaggacctgt ggggtggagac 3060
cagcggccag aggtggagga ccctgaagag ttgtccccag cacttgtagt gtccagttca 3120
cagagctttg tcatcagtgg tggaggcagc actgttacag aaaacgtagt gaattca 3177

```

&lt;210&gt; 39

&lt;211&gt; 1059

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Chimeric hmGluR8/hCaR

&lt;400&gt; 39

```

Met Val Cys Glu Gly Lys Arg Ser Ala Ser Cys Pro Cys Phe Phe Leu
 1           5           10           15
Leu Thr Ala Lys Phe Tyr Trp Ile Leu Thr Met Met Gln Arg Thr His
          20           25           30
Ser Gln Glu Tyr Ala His Ser Ile Arg Val Asp Gly Asp Ile Ile Leu
          35           40           45
Gly Gly Leu Phe Pro Val His Ala Lys Gly Glu Arg Gly Val Pro Cys
          50           55           60

```

67

Gly Glu Leu Lys Lys Glu Lys Gly Ile His Arg Leu Glu Ala Met Leu  
 65 70 75 80  
 Tyr Ala Ile Asp Gln Ile Asn Lys Asp Pro Asp Leu Leu Ser Asn Ile  
 85 90 95  
 Thr Leu Gly Val Arg Ile Leu Asp Thr Cys Ser Arg Asp Thr Tyr Ala  
 100 105 110  
 Leu Glu Gln Ser Leu Thr Phe Val Gln Ala Leu Ile Glu Lys Asp Ala  
 115 120 125  
 Ser Asp Val Lys Cys Ala Asn Gly Asp Pro Pro Ile Phe Thr Lys Pro  
 130 135 140  
 Asp Lys Ile Ser Gly Val Ile Gly Ala Ala Ala Ser Ser Val Ser Ile  
 145 150 155 160  
 Met Val Ala Asn Ile Leu Arg Leu Phe Lys Ile Pro Gln Ile Ser Tyr  
 165 170 175  
 Ala Ser Thr Ala Pro Glu Leu Ser Asp Asn Thr Arg Tyr Asp Phe Phe  
 180 185 190  
 Ser Arg Val Val Pro Pro Asp Ser Tyr Gln Ala Gln Ala Met Val Asp  
 195 200 205  
 Ile Val Thr Ala Leu Gly Trp Asn Tyr Val Ser Thr Leu Ala Ser Glu  
 210 215 220  
 Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg  
 225 230 235 240  
 Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu  
 245 250 255  
 Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr  
 260 265 270  
 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg  
 275 280 285  
 Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu  
 290 295 300  
 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln  
 305 310 315 320  
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala  
 325 330 335  
 Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn  
 340 345 350

Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly  
 355 360 365  
 Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys  
 370 375 380  
 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly  
 385 390 395 400  
 Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu  
 405 410 415  
 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro  
 420 425 430  
 Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala  
 435 440 445  
 Val Asn Phe Asn Gly Ser Ala Gly Thr Pro Val Thr Phe Asn Glu Asn  
 450 455 460  
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn  
 465 470 475 480  
 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His  
 485 490 495  
 Leu Lys Val Glu Asp Met Gln Trp Ala His Arg Glu His Thr His Pro  
 500 505 510  
 Ala Ser Val Cys Ser Leu Pro Cys Lys Pro Gly Glu Arg Lys Lys Thr  
 515 520 525  
 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr  
 530 535 540  
 Asn Tyr Gln Val Asp Glu Leu Ser Cys Glu Leu Cys Pro Leu Asp Gln  
 545 550 555 560  
 Arg Pro Asn Met Asn Arg Thr Gly Cys Gln Leu Ile Pro Ile Ile Lys  
 565 570 575  
 Leu Glu Trp His Ser Pro Trp Ala Val Val Pro Val Phe Val Ala Ile  
 580 585 590  
 Leu Gly Ile Ile Ala Thr Thr Phe Val Ile Val Thr Phe Val Arg Tyr  
 595 600 605  
 Asn Asp Thr Pro Ile Val Arg Ala Ser Gly Arg Glu Leu Ser Tyr Val  
 610 615 620  
 Leu Leu Thr Gly Ile Phe Leu Cys Tyr Ser Ile Thr Phe Leu Met Ile  
 625 630 635 640

69

Ala Ala Pro Asp Thr Ile Ile Cys Ser Phe Arg Arg Val Phe Leu Gly  
 645 650 655  
 Leu Gly Met Cys Phe Ser Tyr Ala Ala Leu Leu Thr Lys Thr Asn Arg  
 660 665 670  
 Ile His Arg Ile Phe Glu Gln Gly Lys Lys Ser Val Thr Ala Pro Lys  
 675 680 685  
 Phe Ile Ser Pro Ala Ser Gln Leu Val Ile Thr Phe Ser Leu Ile Ser  
 690 695 700  
 Val Gln Leu Leu Gly Val Phe Val Trp Phe Val Val Asp Pro Pro His  
 705 710 715 720  
 Ile Ile Ile Asp Tyr Gly Glu Gln Arg Thr Leu Asp Pro Glu Lys Ala  
 725 730 735  
 Arg Gly Val Leu Lys Cys Asp Ile Ser Asp Leu Ser Leu Ile Cys Ser  
 740 745 750  
 Leu Gly Tyr Ser Ile Leu Leu Met Val Thr Cys Thr Val Tyr Ala Ile  
 755 760 765  
 Lys Thr Arg Gly Val Pro Glu Thr Phe Asn Glu Ala Lys Pro Ile Gly  
 770 775 780  
 Phe Thr Met Tyr Thr Thr Cys Ile Ile Trp Leu Ala Phe Ile Pro Ile  
 785 790 795 800  
 Phe Phe Gly Thr Ala Gln Ser Ala Glu Lys Met Tyr Ile Gln Thr Thr  
 805 810 815  
 Thr Leu Thr Val Ser Met Ser Leu Ser Ala Ser Val Ser Leu Gly Met  
 820 825 830  
 Leu Tyr Met Pro Lys Val Tyr Ile Ile Ile Phe His Pro Glu Gln Asn  
 835 840 845  
 Thr Ile Glu Glu Val Arg Cys Ser Thr Ala Ala His Ala Phe Lys Val  
 850 855 860  
 Ala Ala Arg Ala Thr Leu Arg Arg Ser Asn Val Ser Arg Lys Arg Ser  
 865 870 875 880  
 Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro Ser Ser Ser Ile Ser  
 885 890 895  
 Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln Pro Glu Arg Gln Lys  
 900 905 910  
 Gln Gln Gln Pro Leu Ala Leu Thr Gln Gln Glu Gln Gln Gln Pro  
 915 920 925

70

Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln Gln Pro Arg Cys Lys  
 930 935 940  
 Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr Phe Ser Leu Ser Phe  
 945 950 955 960  
 Asp Glu Pro Gln Lys Asn Ala Met Ala His Gly Asn Ser Thr His Gln  
 965 970 975  
 Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr Leu Thr Arg His Gln  
 980 985 990  
 Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp Leu Asp Leu Thr Val  
 995 1000 1005  
 Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly Asp Gln Arg Pro Glu  
 1010 1015 1020  
 Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu Val Val Ser Ser Ser  
 1025 1030 1035 1040  
 Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr Val Thr Glu Asn Val  
 1045 1050 1055  
 Val Asn Ser

<210> 40  
 <211> 4257  
 <212> DNA  
 <213> Artificial Sequence  
 <220>  
 <223> Chimeric mGluR8//CaR\*Gα<sub>i5</sub>  
 <400> 40

atggtatg	cg	agggaaag	cg	atcagcct	ct	tgcccttg	tt	tcttctct	tt	gaccgcca	ag	60
ttctactg	ga	tcctcaca	at	gatgcaa	aga	actcacag	cc	aggagtat	gc	ccattcca	ta	120
cggttgga	tg	gggacatt	at	tttggggg	gt	ctcttccc	tg	tccacgca	aaa	gggagaga	ga	180
ggggtgc	ctt	gtggggag	ct	gaagaagg	aa	aaggggat	tc	acagactg	ga	ggccatgc	tt	240
tatgcaat	tg	accagatta	aa	caaggacc	ct	gatctccc	tt	ccaacatc	ac	tctgggtg	tc	300
cgcatect	cg	acacgtgc	tc	tagggacac	c	tatgcttt	gg	agcagtct	ct	aacattcg	tg	360
caggcatta	aa	tagagaaa	aga	tgcttcgg	at	gtgaagt	gtg	ctaattgg	aga	tccaccat	tt	420
ttcaccaa	agc	ccgacaag	at	ttctggcg	tc	ataggtgc	tg	cagcaagc	tc	cgtgtcca	tc	480
atggttg	cta	acatttta	ag	acttttta	ag	atacctca	aaa	tcagctat	gc	atccacag	cc	540
ccagagcta	aa	gtgataac	ac	caggtatg	ac	ttttctct	tc	gagtgggt	ccc	gcctgact	ccc	600
taccaagc	ccc	aagccatg	gt	ggacatcg	tg	acagcact	gg	gatggaat	ta	tgtttcga	ca	660
ctggcttc	tg	aggggaac	ta	tggtagag	c	ggtgtgg	agg	ccttcacca	ga	gatctcg	agg	720
gagattgg	tg	gtgtttgc	at	tgctcagt	ca	cagaaaat	ccc	cacgtga	acc	aagacctg	ga	780
gaatttg	aaa	aaattatc	aa	acgcctgc	ta	gaaacac	cta	atgctcga	gc	agtgatt	atg	840
tttgcca	atg	aggatgac	at	caggagg	ata	ttggaag	cag	caaaaaa	act	aaaccaa	agt	900
gggcattt	tc	tctggatt	gg	ctcagata	gt	tggggat	cca	aaatagca	ccc	tgtctat	cag	960

caagaggaga	ttgcagaagg	ggctgtgaca	atTTTgcccc	aacgagcatc	aattgatgga	1020
tttgatcgat	actttagaag	ccgaactcct	gccaaataatc	gaagaaatgt	gtgggtttgca	1030
gaattctggg	aggagaattt	tggtcgcaag	ttaggatcac	atgggaaaag	gaacagtcac	1140
ataaagaaat	gcacagggtt	ggagcgaatt	gctcgggatt	catcttatga	acaggaagga	1200
aaggtccaat	ttgtaattga	tgctgtatat	tccatggctt	acgccctgca	caatatgcac	1260
aaagatctct	gccctggata	cattggcctt	tgTccacgaa	tgagtacac	tgatgggaaa	1320
gagctacttg	gttatattcg	ggctgtaaat	tttaattggca	gtgctggcac	tcctgtcact	1380
tttaatgaaa	acggagatgc	tcctggacgt	tatgatattc	tccagtatca	aataaccaac	1440
aaaagcacag	agtacaaaag	catcggccac	tggaaccaatc	agcttcatct	aaaagtggaa	1500
gacatgcagt	gggctcatag	agaacatact	caccggcgct	ctgtctgcag	cctgccgtgt	1560
aagccagggg	agaggaagaa	aacggtgaaa	ggggTccctt	gctgctggca	ctgtgaacgc	1620
tgtgaagggt	acaactacca	ggTggatgag	ctgtcctgtg	aactttgccc	tctggatcag	1680
agacccaaca	tgaaccgcac	aggctgccag	cttatcccca	tcatacaaat	ggagtggcat	1740
tctccctggg	ctgtggtgcc	tgTgtttgtt	gcaatattgg	gaatcatcgc	caccaccttt	1800
gtgatcgTga	cctttgtccg	ctataatgac	acacctatcg	tgagggttc	aggacgcgaa	1860
cttagttacg	tgctcctaac	ggggattttt	ctctgttatt	caatcacgtt	tttaattgatt	1920
gcagcaccag	atacaatcat	atgctccttc	cgacgggtct	tcctaggact	tggtcatgtgt	1980
ttcagctatg	cagcccttct	gaccaaaca	aaccgtatcc	accgaatatt	tgagcagggg	2040
aagaaatctg	tcacagcgcc	caagttcatt	agtccagcat	ctcagctggt	gatcaccttc	2100
agcctcatct	ccgtccagct	ccttgagtg	tttgtctggt	ttgttTgtgga	tcctccccac	2160
atcatcattg	actatggaga	gcagcgga	ctagatccag	agaaggccag	gggagtgtct	2220
aagtgtgaca	tttctgatct	ctcactcatt	tgTtTcactg	gatacagtat	cctcttgatg	2280
gtcacttgta	ctgtttatgc	cattaaaaag	agaggtgtcc	cagagacttt	caatgaagcc	2340
aaacctattg	gatttaccat	gtataaccac	tgcatcattt	ggTtagcttt	catccccatc	2400
ttttttggta	cagcccagtc	agcagaaaag	atgtacatcc	agacaacaac	acttactgtc	2460
tccatgagtt	taagtgtctc	agtatctctg	ggcatgctct	atatgcccaa	ggTttatatt	2520
ataatttttc	atccagaaca	gaataccatc	gaggaggtgc	gttgacgac	cgcagctcac	2580
gctttcaagg	tggtgcccgc	ggccacgctg	cgcgcgagca	acgtctcccgc	caagcggtcc	2640
agcagccttg	gaggctccac	gggatccacc	ccctcctcct	ccatcagcag	caagagcaac	2700
agcgaagacc	cattcccaca	gcccagagag	cagaagcagc	agcagccgct	ggccctaacc	2760
cagcaagagc	agcagcagca	gcccctgacc	ctcccacagc	agcaacgac	tcagcagcag	2820
cccagatgca	agcagaaggt	catctttggc	agcggcacgg	tcaccttctc	actgagcttt	2880
gatgagcctc	agaagaacgc	catggcccac	gggaattcta	cgcaccagaa	ctccctggag	2940
gcccagaaaa	gcagcgatac	gctgacccga	caccagccat	tactcccgc	gcagtgcggg	3000
gaaacggact	tagatctgac	cgtccaggaa	acaggtctgc	aaggacctgt	gggtggagac	3060
cagcggccag	aggtggagga	ccctgaagag	ttgtccccag	cacttgtagt	gtccagttca	3120
cagagccttg	tcatacgtgg	tgagggcagc	actgttacag	aaaacgtagt	gaattcaatg	3180
actctggagt	ccatcatggc	gtgctgcctg	agcagggagg	ccaaggaagc	ccggcgatc	3240
aacgacgaga	tcgagcgga	gctccgcagg	gacaagcggg	acgcccgccg	ggagctcaag	3300
ctgctgctgc	tcgggacagg	agagagtggc	aagagtacgt	ttatcaagca	gatgagaatc	3360
atccatgggt	caggatactc	tgatgaagat	aaaaggggct	tcaccaagct	ggtgtatcag	3420
aacatcttca	cggccatgca	ggccatgatc	agagccatgg	acacactcaa	gatcccatac	3480
aagtatgagc	acaataaggc	tcatagcacaa	ttagttcgag	aagttgatgt	ggagaagggtg	3540
tctgcttttg	agaatccata	tgtagatgca	ataaagagtt	tatggaatga	tcctggaatc	3600
caggaatgct	atgatagacg	acgagaatat	caattatctg	actctaccaa	atactatctt	3660
aatgacttgg	acgcgtagc	tgacctgcc	tacctgccta	cgaacaaga	tgtgcttaga	3720
gttcgagtec	ccaccacagg	gatcatcgaa	tacctcttg	acttacaag	tgctattttc	3780
agaatggctg	atgtaggggg	ccaaaggTca	gagagaagaa	aatggataca	ctgctttgaa	3840
aatgtcacct	ctatcatgtt	tctagttagc	cttagtgaat	atgatcaagt	tctcgtggag	3900
tcagacaatg	agaaccgaat	ggaggaaaag	aaggctctct	ttagaacaat	tatcacatac	3960
ccctggttcc	agaactcctc	ggTtattctg	ttcttaaaca	agaaagatct	tctagaggag	4020
aaaatcatgt	attcccatct	agtcgactac	ttcccagaat	atgatggacc	ccagagagat	4080
gcccaggcag	cccgagaatt	cattctgaag	atgttcgtgg	acctgaaccc	agacagtgac	4140
aaaattatct	actccactt	cacgtgcgcc	acagacaccg	agaatatccg	ctttgtcttt	4200
gctgccgtca	aggacaccat	cctccagttg	aacctgaagg	actgcggctc	gttctaa	4257

<210> 41  
 <211> 1418  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Chimeric mGluR8//CaR\*Gα<sub>i5</sub>

<400> 41

Met	Val	Cys	Glu	Gly	Lys	Arg	Ser	Ala	Ser	Cys	Pro	Cys	Phe	Phe	Leu	1	5	10	15
Leu	Thr	Ala	Lys	Phe	Tyr	Trp	Ile	Leu	Thr	Met	Met	Gln	Arg	Thr	His	20	25	30	
Ser	Gln	Glu	Tyr	Ala	His	Ser	Ile	Arg	Val	Asp	Gly	Asp	Ile	Ile	Leu	35	40	45	
Gly	Gly	Leu	Phe	Pro	Val	His	Ala	Lys	Gly	Glu	Arg	Gly	Val	Pro	Cys	50	55	60	
Gly	Glu	Leu	Lys	Lys	Glu	Lys	Gly	Ile	His	Arg	Leu	Glu	Ala	Met	Leu	65	70	75	80
Tyr	Ala	Ile	Asp	Gln	Ile	Asn	Lys	Asp	Pro	Asp	Leu	Leu	Ser	Asn	Ile	85	90	95	
Thr	Leu	Gly	Val	Arg	Ile	Leu	Asp	Thr	Cys	Ser	Arg	Asp	Thr	Tyr	Ala	100	105	110	
Leu	Glu	Gln	Ser	Leu	Thr	Phe	Val	Gln	Ala	Leu	Ile	Glu	Lys	Asp	Ala	115	120	125	
Ser	Asp	Val	Lys	Cys	Ala	Asn	Gly	Asp	Pro	Pro	Ile	Phe	Thr	Lys	Pro	130	135	140	
Asp	Lys	Ile	Ser	Gly	Val	Ile	Gly	Ala	Ala	Ala	Ser	Ser	Val	Ser	Ile	145	150	155	160
Met	Val	Ala	Asn	Ile	Leu	Arg	Leu	Phe	Lys	Ile	Pro	Gln	Ile	Ser	Tyr	165	170	175	
Ala	Ser	Thr	Ala	Pro	Glu	Leu	Ser	Asp	Asn	Thr	Arg	Tyr	Asp	Phe	Phe	180	185	190	
Ser	Arg	Val	Val	Pro	Pro	Asp	Ser	Tyr	Gln	Ala	Gln	Ala	Met	Val	Asp	195	200	205	
Ile	Val	Thr	Ala	Leu	Gly	Trp	Asn	Tyr	Val	Ser	Thr	Leu	Ala	Ser	Glu	210	215	220	

Gly Asn Tyr Gly Glu Ser Gly Val Glu Ala Phe Thr Gln Ile Ser Arg  
 225 230 235 240  
 Glu Ile Gly Gly Val Cys Ile Ala Gln Ser Gln Lys Ile Pro Arg Glu  
 245 250 255  
 Pro Arg Pro Gly Glu Phe Glu Lys Ile Ile Lys Arg Leu Leu Glu Thr  
 260 265 270  
 Pro Asn Ala Arg Ala Val Ile Met Phe Ala Asn Glu Asp Asp Ile Arg  
 275 280 285  
 Arg Ile Leu Glu Ala Ala Lys Lys Leu Asn Gln Ser Gly His Phe Leu  
 290 295 300  
 Trp Ile Gly Ser Asp Ser Trp Gly Ser Lys Ile Ala Pro Val Tyr Gln  
 305 310 315 320  
 Gln Glu Glu Ile Ala Glu Gly Ala Val Thr Ile Leu Pro Lys Arg Ala  
 325 330 335  
 Ser Ile Asp Gly Phe Asp Arg Tyr Phe Arg Ser Arg Thr Leu Ala Asn  
 340 345 350  
 Asn Arg Arg Asn Val Trp Phe Ala Glu Phe Trp Glu Glu Asn Phe Gly  
 355 360 365  
 Cys Lys Leu Gly Ser His Gly Lys Arg Asn Ser His Ile Lys Lys Cys  
 370 375 380  
 Thr Gly Leu Glu Arg Ile Ala Arg Asp Ser Ser Tyr Glu Gln Glu Gly  
 385 390 395 400  
 Lys Val Gln Phe Val Ile Asp Ala Val Tyr Ser Met Ala Tyr Ala Leu  
 405 410 415  
 His Asn Met His Lys Asp Leu Cys Pro Gly Tyr Ile Gly Leu Cys Pro  
 420 425 430  
 Arg Met Ser Thr Ile Asp Gly Lys Glu Leu Leu Gly Tyr Ile Arg Ala  
 435 440 445  
 Val Asn Phe Asn Gly Ser Ala Gly Thr Pro Val Thr Phe Asn Glu Asn  
 450 455 460  
 Gly Asp Ala Pro Gly Arg Tyr Asp Ile Phe Gln Tyr Gln Ile Thr Asn  
 465 470 475 480  
 Lys Ser Thr Glu Tyr Lys Val Ile Gly His Trp Thr Asn Gln Leu His  
 485 490 495  
 Leu Lys Val Glu Asp Met Gln Trp Ala His Arg Glu His Thr His Pro  
 500 505 510



Ala Ser Val Cys Ser Leu Pro Cys Lys Pro Gly Glu Arg Lys Lys Thr  
 515 520 525  
 Val Lys Gly Val Pro Cys Cys Trp His Cys Glu Arg Cys Glu Gly Tyr  
 530 535 540  
 Asn Tyr Gln Val Asp Glu Leu Ser Cys Glu Leu Cys Pro Leu Asp Gln  
 545 550 555 560  
 Arg Pro Asn Met Asn Arg Thr Gly Cys Gln Leu Ile Pro Ile Ile Lys  
 565 570 575  
 Leu Glu Trp His Ser Pro Trp Ala Val Val Pro Val Phe Val Ala Ile  
 580 585 590  
 Leu Gly Ile Ile Ala Thr Thr Phe Val Ile Val Thr Phe Val Arg Tyr  
 595 600 605  
 Asn Asp Thr Pro Ile Val Arg Ala Ser Gly Arg Glu Leu Ser Tyr Val  
 610 615 620  
 Leu Leu Thr Gly Ile Phe Leu Cys Tyr Ser Ile Thr Phe Leu Met Ile  
 625 630 635 640  
 Ala Ala Pro Asp Thr Ile Ile Cys Ser Phe Arg Arg Val Phe Leu Gly  
 645 650 655  
 Leu Gly Met Cys Phe Ser Tyr Ala Ala Leu Leu Thr Lys Thr Asn Arg  
 660 665 670  
 Ile His Arg Ile Phe Glu Gln Gly Lys Lys Ser Val Thr Ala Pro Lys  
 675 680 685  
 Phe Ile Ser Pro Ala Ser Gln Leu Val Ile Thr Phe Ser Leu Ile Ser  
 690 695 700  
 Val Gln Leu Leu Gly Val Phe Val Trp Phe Val Val Asp Pro Pro His  
 705 710 715 720  
 Ile Ile Ile Asp Tyr Gly Glu Gln Arg Thr Leu Asp Pro Glu Lys Ala  
 725 730 735  
 Arg Gly Val Leu Lys Cys Asp Ile Ser Asp Leu Ser Leu Ile Cys Ser  
 740 745 750  
 Leu Gly Tyr Ser Ile Leu Leu Met Val Thr Cys Thr Val Tyr Ala Ile  
 755 760 765  
 Lys Thr Arg Gly Val Pro Glu Thr Phe Asn Glu Ala Lys Pro Ile Gly  
 770 775 780  
 Phe Thr Met Tyr Thr Thr Cys Ile Ile Trp Leu Ala Phe Ile Pro Ile  
 785 790 795 800

75

Phe Phe Gly Thr Ala Gln Ser Ala Glu Lys Met Tyr Ile Gln Thr Thr  
 805 810 815  
 Thr Leu Thr Val Ser Met Ser Leu Ser Ala Ser Val Ser Leu Gly Met  
 820 825 830  
 Leu Tyr Met Pro Lys Val Tyr Ile Ile Ile Phe His Pro Glu Gln Asn  
 835 840 845  
 Thr Ile Glu Glu Val Arg Cys Ser Thr Ala Ala His Ala Phe Lys Val  
 850 855 860  
 Ala Ala Arg Ala Thr Leu Arg Arg Ser Asn Val Ser Arg Lys Arg Ser  
 865 870 875 880  
 Ser Ser Leu Gly Gly Ser Thr Gly Ser Thr Pro Ser Ser Ser Ile Ser  
 885 890 895  
 Ser Lys Ser Asn Ser Glu Asp Pro Phe Pro Gln Pro Glu Arg Gln Lys  
 900 905 910  
 Gln Gln Gln Pro Leu Ala Leu Thr Gln Gln Glu Gln Gln Gln Gln Pro  
 915 920 925  
 Leu Thr Leu Pro Gln Gln Gln Arg Ser Gln Gln Gln Pro Arg Cys Lys  
 930 935 940  
 Gln Lys Val Ile Phe Gly Ser Gly Thr Val Thr Phe Ser Leu Ser Phe  
 945 950 955 960  
 Asp Glu Pro Gln Lys Asn Ala Met Ala His Gly Asn Ser Thr His Gln  
 965 970 975  
 Asn Ser Leu Glu Ala Gln Lys Ser Ser Asp Thr Leu Thr Arg His Gln  
 980 985 990  
 Pro Leu Leu Pro Leu Gln Cys Gly Glu Thr Asp Leu Asp Leu Thr Val  
 995 1000 1005  
 Gln Glu Thr Gly Leu Gln Gly Pro Val Gly Gly Asp Gln Arg Pro Glu  
 1010 1015 1020  
 Val Glu Asp Pro Glu Glu Leu Ser Pro Ala Leu Val Val Ser Ser Ser  
 1025 1030 1035 1040  
 Gln Ser Phe Val Ile Ser Gly Gly Gly Ser Thr Val Thr Glu Asn Val  
 1045 1050 1055  
 Val Asn Ser Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu Ser Glu  
 1060 1065 1070  
 Glu Ala Lys Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu  
 1075 1080 1085

Arg Arg Asp Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Leu  
 1090 1095 1100  
 Gly Thr Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile  
 1105 1110 1115 1120  
 Ile His Gly Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys  
 1125 1130 1135  
 Leu Val Tyr Gln Asn Ile Phe Thr Ala Met Gln Ala Met Ile Arg Ala  
 1140 1145 1150  
 Met Asp Thr Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His  
 1155 1160 1165  
 Ala Gln Leu Val Arg Glu Val Asp Val Glu Lys Val Ser Ala Phe Glu  
 1170 1175 1180  
 Asn Pro Tyr Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly Ile  
 1185 1190 1195 1200  
 Gln Glu Cys Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser Thr  
 1205 1210 1215  
 Lys Tyr Tyr Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr Leu  
 1220 1225 1230  
 Pro Thr Gln Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr Gly Ile  
 1235 1240 1245  
 Ile Glu Tyr Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met Val Asp  
 1250 1255 1260  
 Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu  
 1265 1270 1275 1280  
 Asn Val Thr Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln  
 1285 1290 1295  
 Val Leu Val Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala  
 1300 1305 1310  
 Leu Phe Arg Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val  
 1315 1320 1325  
 Ile Leu Phe Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr  
 1330 1335 1340  
 Ser His Leu Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp  
 1345 1350 1355 1360  
 Ala Gln Ala Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn  
 1365 1370 1375

Pro Asp Ser Asp Lys Ile Ile Tyr Ser His Phe Thr Cys Ala Thr Asp  
1380 1385 1390

Thr Glu Asn Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr Ile Leu  
1395 1400 1405

Gln Leu Asn Leu Lys Asp Cys Gly Leu Phe  
1410 1415

<210> 42  
<211> 3909  
<212> DNA  
<213> Artificial Sequence  
  
<220>  
<223> Chimeric GABA-BR2\*Gqo5  
  
<400> 42

atggcttccc	cgcgagctc	cgggcagccc	gggcccgcgc	cgccgcgcgc	accgcgcgcc	60
gcgcgcctgc	tactgctact	gctgctgccc	ctgctgctgc	ctctggcgcc	cggggcctgg	120
ggctgggcgc	ggggcgcccc	ccggccgcgc	cccagcagcc	cgccgctctc	catcatgggc	180
ctcatgccgc	tcaccaagga	ggtggccaag	ggcagcatcg	ggcgcggtgt	gctccccgcc	240
gtggaactgg	ccatcgagca	gatccgcaac	gagtcactcc	tgccgcctta	cttcctcgac	300
ctgcggtctc	atgacacgga	gtgcgacaac	gcaaaagggt	tgaaagcctt	ctacgatgca	360
ataaaatacg	ggccgaacca	cttgatgggt	tttggaggcg	tctgtccatc	cgtcacatcc	420
atcattgcag	agtcctctca	aggctggaat	ctggtgcagc	tttcttttgc	tgcaaccacg	480
cctgttctag	ccgataagaa	aaaataccct	tatttcttcc	ggaccgtccc	atcagacaat	540
gcggtgaatc	cagccattct	gaagttgtct	aagcactacc	agtgggaagcg	cgtgggcacg	600
ctgacgcaag	acgttcagag	gttctctgag	gtgcggaatg	acctgactgg	agttctgtat	660
ggcgaggaca	ttgagatttc	agacaccgag	agcttctcca	acgatccctg	taccagtgtc	720
aaaaagctga	aggggaatga	tgtgcggatc	atccttgccc	agtttgacca	gaatatggca	780
gcaaaagtgt	tctgttgtgc	atacaggagg	aacatgtatg	gtagtaata	tcagtggatc	840
attccgggct	ggtacgagcc	ttcttggtgg	gagcagggtc	acacggaagc	caactcatcc	900
cgctgcctcc	ggaagaatct	gcttgctgcc	atggagggct	acattggcgt	ggatttcgag	960
cccctgagct	ccaagcagat	caagaccatc	tcaggaaaag	ctccacagca	gtatgagaga	1020
gagtacaaca	acaagcggtc	aggcgtgggg	cccagcaagt	tccacgggta	cgcctacgat	1080
ggcatctggg	tcacgcgcaa	gacactgcag	agggccatgg	agacactgca	tgccagcagc	1140
cggcaccagc	ggatccagga	cttcaactac	acggaccaca	cgctgggcag	gatcatcctc	1200
aatggccatga	acgagaccaa	cttcttcggg	gtcacgggtc	aagttgtatt	ccggaatggg	1260
gagagaatgg	ggaccattaa	atttactcaa	tttcaagaca	gcaggagagt	gaaggtggga	1320
gagtacaacg	ctgtggccga	cacactggag	atcatcaatg	acaccatcag	gttccaagga	1380
tccgaaccac	caaaagacaa	gaccatcatc	ctggagcagc	tgcggaagat	ctccctacct	1440
ctctacagca	tcctctctgc	cctcaccatc	ctcgggatga	tcattggccag	tgcttttctc	1500
ttcttcaaca	tcaagaaccg	gaatcagaag	ctcataaaga	tgctcagatc	atacatgaac	1560
aaccttatca	tccttgaggg	gatgctctcc	tatgcttcca	tatttctctt	tggccttgat	1620
ggatcctttg	tctctgaaaa	gacctttgaa	acactttgca	ccgtcaggac	ctggattctc	1680
accgtgggct	acacgaccgc	ttttggggcc	atgtttgcaa	agacctggag	agtcacagcc	1740
atcttcaaaa	atgtgaaaat	gaagaagaag	atcatcaagg	accagaaaact	gcttgatgat	1800
gtggggggca	tgctgctgat	cgacctgtgt	atcctgatct	gctggcaggc	tggtggacccc	1860
ctgcgaagga	cagtggagaa	gtacagcatg	gagccggacc	cagcaggacg	ggatatctcc	1920
atccgcccctc	tcctggagca	ctgtgagaac	acccatataga	ccatctggct	tggtcatcgtc	1980
tatgcctaca	agggaactct	catgttgttc	ggttgtttct	tagcttgagg	gaccgcgaac	2040

```

gtcagcatcc ccgcaactcaa cgacagcaag tacatcgga tgagtgtcta caacgtggg 2100
atcatgtgca tcatcggggc cgctgtctcc ttctgaccc gggaccagcc caatgtgcag 2160
ttctgcatcg tggctctggt catcatcttc tgcagacca tcaccctctg cctggtattc 2220
gtgccgaagc tcatcaccct gagaacaaac ccagatgcag caacgcagaa caggcgattc 2280
cagttcactc agaatcagaa gaaagaagat tctaaaacgt ccacctcggg caccagtgtg 2340
aaccaagcca gcacatcccg cctggagggc ctacagtcag aaaaccatcg cctgcgaatg 2400
aagatcacag agctggataa agacttggaa gaggtcacca tgcagctgca ggacacacca 2460
gaaaagacca cctacattaa acagaaccac taccaagagc tcaatgacat cctcaacctg 2520
ggaaacttca ctgagagcac agatggagga aaggccattt taaaaaatca cctcgatcaa 2580
aatccccagc tacagtggaa cacaacagag ccctctcgaa catgcaaaga tcctatagaa 2640
gatataaact ctccagaaca catccagcgt cggctgtccc tccagctccc catcctccac 2700
cacgcctacc tcccattccat cggaggcgtg gacgccagct gtgtcagccc ctgctcagc 2760
cccccgcca gcccccgcca cagacatgtg ccaccctcct tccgagtcac ggtctcgggc 2820
ctggcggccg ccatgactct ggagtcacat atggcgtgct gcctgagcga ggaggccaag 2880
gaagcccggc ggatcaacga cgagatcgag cggcagctcc gcagggacaa gcgggacgcc 2940
cgccgggagc tcaagctgct gctgctcggg acaggagaga gtggcaagag tacgtttatc 3000
aagcagatga gaatcatcca tgggtcagga tactctgatg aagataaaag gggcttcacc 3060
aagctggtgt atcagaacat cttcacggcc atgcaggcca tgatcagagc catggacaca 3120
ctcaagatcc catacaagta tgagcacaat aaggctcatg cacaattagt tgcagaagtt 3180
gatgtggaga aggtgtctgc ttttgagaat ccatatgtag atgcaataaa gagtttatgg 3240
aatgatcctg gaatccagga atgctatgat agacgacgag aatatcaatt atctgactct 3300
accaaatact atcttaatga cttggaccgc gtagctgacc ctgcctacct gcctacgcaa 3360
caagatgtgc ttagagttcg agtccccacc acagggatca tcgaataccc ctttgactta 3420
caaagtgtca ttttcagaat ggtcgatgta gggggccaaa ggtcagagag aagaaaatgg 3480
atacactgct ttgaaaatgt caccctctatc atgtttctag tagcgcttag tgaatatgat 3540
caagttctgg tggagtcaga caatgagaac cgaatggagg aaagcaaggc tctctttaga 3600
acaattatca catacccttg gttccagaac tcctcggtta ttctgttctt aaacaagaaa 3660
gatcttctag aggagaaaat catgtattcc catctagtcg actacttccc agaatatgat 3720
ggaccccgaga gagatgccc ggcagcccga gaattcatte tgaagatgtt cgtggacctg 3780
aaccagaca gtgacaaaat taactactcc cacttcacgt gcgccacaga caccgagaat 3840
atccgctttg tctttgctgc cgtcaaaggac accatcctcc agttgaacct gaagggctgc 3900
ggtctgtac 3909

```

<210> 43  
 <211> 1303  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Chimeric GABA-BR2\*Gqo5

<400> 43

```

Met Ala Ser Pro Arg Ser Ser Gly Gln Pro Gly Pro Pro Pro Pro Pro
1           5           10           15

Pro Pro Pro Pro Ala Arg Leu Leu Leu Leu Leu Leu Leu Pro Leu Leu
20           25           30

Leu Pro Leu Ala Pro Gly Ala Trp Gly Trp Ala Arg Gly Ala Pro Arg
35           40           45

```

79

Pro Pro Pro Ser Ser Pro Pro Leu Ser Ile Met Gly Leu Met Pro Leu  
 50 55 60  
 Thr Lys Glu Val Ala Lys Gly Ser Ile Gly Arg Gly Val Leu Pro Ala  
 65 70 75 80  
 Val Glu Leu Ala Ile Glu Gln Ile Arg Asn Glu Ser Leu Leu Arg Pro  
 85 90 95  
 Tyr Phe Leu Asp Leu Arg Leu Tyr Asp Thr Glu Cys Asp Asn Ala Lys  
 100 105 110  
 Gly Leu Lys Ala Phe Tyr Asp Ala Ile Lys Tyr Gly Pro Asn His Leu  
 115 120 125  
 Met Val Phe Gly Gly Val Cys Pro Ser Val Thr Ser Ile Ile Ala Glu  
 130 135 140  
 Ser Leu Gln Gly Trp Asn Leu Val Gln Leu Ser Phe Ala Ala Thr Thr  
 145 150 155 160  
 Pro Val Leu Ala Asp Lys Lys Lys Tyr Pro Tyr Phe Phe Arg Thr Val  
 165 170 175  
 Pro Ser Asp Asn Ala Val Asn Pro Ala Ile Leu Lys Leu Leu Lys His  
 180 185 190  
 Tyr Gln Trp Lys Arg Val Gly Thr Leu Thr Gln Asp Val Gln Arg Phe  
 195 200 205  
 Ser Glu Val Arg Asn Asp Leu Thr Gly Val Leu Tyr Gly Glu Asp Ile  
 210 215 220  
 Glu Ile Ser Asp Thr Glu Ser Phe Ser Asn Asp Pro Cys Thr Ser Val  
 225 230 235 240  
 Lys Lys Leu Lys Gly Asn Asp Val Arg Ile Ile Leu Gly Gln Phe Asp  
 245 250 255  
 Gln Asn Met Ala Ala Lys Val Phe Cys Cys Ala Tyr Glu Glu Asn Met  
 260 265 270  
 Tyr Gly Ser Lys Tyr Gln Trp Ile Ile Pro Gly Trp Tyr Glu Pro Ser  
 275 280 285  
 Trp Trp Glu Gln Val His Thr Glu Ala Asn Ser Ser Arg Cys Leu Arg  
 290 295 300  
 Lys Asn Leu Leu Ala Ala Met Glu Gly Tyr Ile Gly Val Asp Phe Glu  
 305 310 315 320  
 Pro Leu Ser Ser Lys Gln Ile Lys Thr Ile Ser Gly Lys Thr Pro Gln  
 325 330 335

Gln Tyr Glu Arg Glu Tyr Asn Asn Lys Arg Ser Gly Val Gly Pro Ser  
 340 345 350  
 Lys Phe His Gly Tyr Ala Tyr Asp Gly Ile Trp Val Ile Ala Lys Thr  
 355 360 365  
 Leu Gln Arg Ala Met Glu Thr Leu His Ala Ser Ser Arg His Gln Arg  
 370 375 380  
 Ile Gln Asp Phe Asn Tyr Thr Asp His Thr Leu Gly Arg Ile Ile Leu  
 385 390 395 400  
 Asn Ala Met Asn Glu Thr Asn Phe Phe Gly Val Thr Gly Gln Val Val  
 405 410 415  
 Phe Arg Asn Gly Glu Arg Met Gly Thr Ile Lys Phe Thr Gln Phe Gln  
 420 425 430  
 Asp Ser Arg Glu Val Lys Val Gly Glu Tyr Asn Ala Val Ala Asp Thr  
 435 440 445  
 Leu Glu Ile Ile Asn Asp Thr Ile Arg Phe Gln Gly Ser Glu Pro Pro  
 450 455 460  
 Lys Asp Lys Thr Ile Ile Leu Glu Gln Leu Arg Lys Ile Ser Leu Pro  
 465 470 475 480  
 Leu Tyr Ser Ile Leu Ser Ala Leu Thr Ile Leu Gly Met Ile Met Ala  
 485 490 495  
 Ser Ala Phe Leu Phe Phe Asn Ile Lys Asn Arg Asn Gln Lys Leu Ile  
 500 505 510  
 Lys Met Ser Ser Pro Tyr Met Asn Asn Leu Ile Ile Leu Gly Gly Met  
 515 520 525  
 Leu Ser Tyr Ala Ser Ile Phe Leu Phe Gly Leu Asp Gly Ser Phe Val  
 530 535 540  
 Ser Glu Lys Thr Phe Glu Thr Leu Cys Thr Val Arg Thr Trp Ile Leu  
 545 550 555 560  
 Thr Val Gly Tyr Thr Thr Ala Phe Gly Ala Met Phe Ala Lys Thr Trp  
 565 570 575  
 Arg Val His Ala Ile Phe Lys Asn Val Lys Met Lys Lys Lys Ile Ile  
 580 585 590  
 Lys Asp Gln Lys Leu Leu Val Ile Val Gly Gly Met Leu Leu Ile Asp  
 595 600 605  
 Leu Cys Ile Leu Ile Cys Trp Gln Ala Val Asp Pro Leu Arg Arg Thr  
 610 615 620

81

Val	Glu	Lys	Tyr	Ser	Met	Glu	Pro	Asp	Pro	Ala	Gly	Arg	Asp	Ile	Ser	625	630	635	640
Ile	Arg	Pro	Leu	Leu	Glu	His	Cys	Glu	Asn	Thr	His	Met	Thr	Ile	Trp	645	650	655	
Leu	Gly	Ile	Val	Tyr	Ala	Tyr	Lys	Gly	Leu	Leu	Met	Leu	Phe	Gly	Cys	660	665	670	
Phe	Leu	Ala	Trp	Glu	Thr	Arg	Asn	Val	Ser	Ile	Pro	Ala	Leu	Asn	Asp	675	680	685	
Ser	Lys	Tyr	Ile	Gly	Met	Ser	Val	Tyr	Asn	Val	Gly	Ile	Met	Cys	Ile	690	695	700	
Ile	Gly	Ala	Ala	Val	Ser	Phe	Leu	Thr	Arg	Asp	Gln	Pro	Asn	Val	Gln	705	710	715	720
Phe	Cys	Ile	Val	Ala	Leu	Val	Ile	Ile	Phe	Cys	Ser	Thr	Ile	Thr	Leu	725	730	735	
Cys	Leu	Val	Phe	Val	Pro	Lys	Leu	Ile	Thr	Leu	Arg	Thr	Asn	Pro	Asp	740	745	750	
Ala	Ala	Thr	Gln	Asn	Arg	Arg	Phe	Gln	Phe	Thr	Gln	Asn	Gln	Lys	Lys	755	760	765	
Glu	Asp	Ser	Lys	Thr	Ser	Thr	Ser	Val	Thr	Ser	Val	Asn	Gln	Ala	Ser	770	775	780	
Thr	Ser	Arg	Leu	Glu	Gly	Leu	Gln	Ser	Glu	Asn	His	Arg	Leu	Arg	Met	785	790	795	800
Lys	Ile	Thr	Glu	Leu	Asp	Lys	Asp	Leu	Glu	Glu	Val	Thr	Met	Gln	Leu	805	810	815	
Gln	Asp	Thr	Pro	Glu	Lys	Thr	Thr	Tyr	Ile	Lys	Gln	Asn	His	Tyr	Gln	820	825	830	
Glu	Leu	Asn	Asp	Ile	Leu	Asn	Leu	Gly	Asn	Phe	Thr	Glu	Ser	Thr	Asp	835	840	845	
Gly	Gly	Lys	Ala	Ile	Leu	Lys	Asn	His	Leu	Asp	Gln	Asn	Pro	Gln	Leu	850	855	860	
Gln	Trp	Asn	Thr	Thr	Glu	Pro	Ser	Arg	Thr	Cys	Lys	Asp	Pro	Ile	Glu	865	870	875	880
Asp	Ile	Asn	Ser	Pro	Glu	His	Ile	Gln	Arg	Arg	Leu	Ser	Leu	Gln	Leu	885	890	895	
Pro	Ile	Leu	His	His	Ala	Tyr	Leu	Pro	Ser	Ile	Gly	Gly	Val	Asp	Ala	900	905	910	



Ser Cys Val Ser Pro Cys Val Ser Pro Thr Ala Ser Pro Arg His Arg  
 915 920 925  
 His Val Pro Pro Ser Phe Arg Val Met Val Ser Gly Leu Ala Ala Ala  
 930 935 940  
 Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu Ser Glu Glu Ala Lys  
 945 950 955 960  
 Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu Arg Arg Asp  
 965 970 975  
 Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Leu Gly Thr Gly  
 980 985 990  
 Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly  
 995 1000 1005  
 Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr  
 1010 1015 1020  
 Gln Asn Ile Phe Thr Ala Met Gln Ala Met Ile Arg Ala Met Asp Thr  
 1025 1030 1035 1040  
 Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His Ala Gln Leu  
 1045 1050 1055  
 Val Arg Glu Val Asp Val Glu Lys Val Ser Ala Phe Glu Asn Pro Tyr  
 1060 1065 1070  
 Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly Ile Gln Glu Cys  
 1075 1080 1085  
 Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser Thr Lys Tyr Tyr  
 1090 1095 1100  
 Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr Leu Pro Thr Gln  
 1105 1110 1115 1120  
 Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr Gly Ile Ile Glu Tyr  
 1125 1130 1135  
 Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met Val Asp Val Gly Gly  
 1140 1145 1150  
 Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu Asn Val Thr  
 1155 1160 1165  
 Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln Val Leu Val  
 1170 1175 1180  
 Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg  
 1185 1190 1195 1200

Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val Ile Leu Phe  
1205 1210 1215

Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr Ser His Leu  
1220 1225 1230

Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp Ala Gln Ala  
1235 1240 1245

Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn Pro Asp Ser  
1250 1255 1260

Asp Lys Ile Asn Tyr Ser His Phe Thr Cys Ala Thr Asp Thr Glu Asn  
1265 1270 1275 1280

Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr Ile Leu Gln Leu Asn  
1285 1290 1295

Leu Lys Gly Cys Gly Leu Tyr  
1300

<210> 44

<211> 3969

<212> DNA

<213> Artificial Sequence

<220>

<223> Chimeric GABA-BR1a\*Gqo5

<400> 44

atgttgctgc	tgctgctact	ggcgccactc	ttcctccgcc	ccccggggcg	ggcgggggcg	60
cagacccccca	acgccacctc	agaaggttgc	cagatcatac	acccgccctg	ggaagggggc	120
atcaggtagc	ggggcctgac	tcgggaccag	gtgaaggcta	tcaacttcct	gccagtggac	180
tatgagattg	agtatgtgtg	ccggggggag	cgcgaggtgg	tggggcccaa	ggcccgcaag	240
tgcttggcca	acggctcctg	gacagatatg	gacacaccca	gccgctgtgt	ccgaatctgc	300
tccaagtctt	atttgaccct	ggaaaatggg	aaggttttcc	tgacgggtgg	ggacctccca	360
gctctggacg	gagcccgggt	ggatttccgg	tgtgaccccg	acttccatct	ggtgggcagc	420
tcccggagca	tctgtagtca	gggccagtgg	agcaccacca	agccccactg	ccaggtgaat	480
cgaacgccac	actcagaacg	gcgcgcagtg	tacatcgggg	cactgtttcc	catgagcggg	540
ggctggccag	ggggccaggc	ctgccagccc	gcggtggaga	tggcgtgga	ggacgtgaat	600
agccgcaggg	acatcctgcc	ggactatgag	ctcaagctca	tccaccacga	cagcaagtgt	660
gatccaggcc	aagccaccaa	gtacctatat	gagctgctct	acaacgaccc	tatcaagatc	720
atccttatgc	ctggctgcag	ctctgtctcc	acgctgggtg	ctgaggctgc	taggatgtgg	780
aacctcattg	tgctttccta	tggctccagc	tcaccagccc	tgtcaaaccg	gcagcgtttc	840
cccactttct	tccgaacgca	cccatcagcc	acactccaca	accctaccgg	cgtgaaactc	900
tttgaaaagt	ggggctggaa	gaagattgct	accatccagc	agaccactga	ggtcttcact	960
tcgactctgg	acgacctgga	ggaacgagtg	aaggaggctg	gaattgagat	tactttccgc	1020
cagagtttct	tctcagatcc	agctgtgccc	gtcaaaaacc	tgaagcgcca	ggatgcccga	1080
atcatcgtgg	gacttttcta	tgagactgaa	gcccggaaag	ttttttgtga	ggtgtacaag	1140
gagcgtctct	ttgggaagaa	gtacgtctgg	ttcctcattg	ggtggtatgc	tgacaattgg	1200
ttcaagatct	acgacccttc	tatcaactgc	acagtggatg	agatgactga	ggcgggtggag	1260

ggccacatca	caactgagat	tgtcatgctg	aatcctgcc	ataccgcgag	catttccaac	1320
atgacatccc	aggaatttgt	ggagaaacta	accaagcgac	tgaaaagaca	ccctgaggag	1380
acaggaggct	tccaggaggc	accgctggcc	tatgatgcc	tctgggcctt	ggcactggcc	1440
ctgaacaaga	catctggagg	aggcggccgt	tctgggtgtc	gcctggagga	cttcaactac	1500
aacaaccaga	ccattaccga	ccaaatctac	cgggcaatga	actcttcgtc	ctttgagggg	1560
gtctctggcc	atgtggtgtt	tgatgccagc	ggctctcgga	tggcatggac	gcttatcgag	1620
cagcttcagg	gtggcagcta	caagaagatt	ggctactatg	acagcaccaa	ggatgatctt	1680
tcctgggtcca	aaacagataa	atggattgga	gggtccccc	cagctgacca	gacctgggtc	1740
atcaagacat	tccgcttcct	gtcacagaaa	ctctttatct	ccgtctcagt	tctctccagc	1800
ctgggcattg	tcttagctgt	tgtctgtctg	tcctttaaca	tctacaactc	acatgtccgt	1860
tatatccaga	actcacagcc	caacctgaac	aacctgactg	ctgtgggctg	ctcactggct	1920
ttagctgctg	tcttccccct	ggggctcgat	ggttaccaca	ttgggaggaa	ccagtttctt	1980
ttcgtctgcc	aggcccgcc	ctggctcctg	ggcctgggct	ttagtctggg	ctacggttcc	2040
atgttcacca	agatttggtg	gggtccacacg	gtcttcacaa	agaagggaaga	aaagaaggag	2100
tggaggaaga	ctctggaacc	ctggaagctg	tatgccacag	tgggcctgct	ggtgggcatg	2160
gatgtcctca	ctctcgccat	ctggcagatc	gtggaccctc	tgcaccggac	cattgagaca	2220
tttgccaagg	aggaacctaa	ggaagatatt	gacgtctcta	ttctgcccc	gctggagcat	2280
tgcagctcca	ggaagatgaa	tacatggctt	ggcattttct	atggttacaa	ggggctgctg	2340
ctgctgtggg	gaatcttctt	tgtttatgag	accaagagtg	tgtccactga	gaagatcaat	2400
gatcacccgg	ctgtgggcat	ggctatctac	aatgtggcag	tcctgtgcct	catcactgct	2460
cctgtcacca	tgattctgtc	cagccagcag	gatgcagcct	ttgcctttgc	ctctcttgcc	2520
atagttttct	cctcctatat	cactcttggt	gtgctctttg	tgcccaagat	gcgcaggctg	2580
atcacccgag	gggaatggca	gtcggaggcg	caggacacca	tgaagacagg	gtcatcgacc	2640
aacaacaacg	aggaggagaa	gtcccggctg	ttggagaagg	agaaccgtga	actggaaaag	2700
atcattgtctg	agaaagagga	gcgtgtctct	gaactgcgcc	atcaactcca	gtctcgccag	2760
cagctccgct	cccggcgcca	cccaccgaca	cccccagaac	cctctggggg	cctgcccgag	2820
ggacccccctg	agccccccga	ccggcttagc	tgtgatggga	gtcgagtgca	tttgctttat	2880
aaggcggccg	ccatgactct	ggagtccatc	atggcgtgct	gcctgagcga	ggaggccaag	2940
gaagcccggc	ggatcaacga	cgagatcgag	cggcagctcc	gcagggacaa	gcgggacgcc	3000
cgccgggagc	tcaagctgct	gctgctcggg	acaggagaga	gtggcaagag	tacgtttatc	3060
aagcagatga	gaatcatcca	tgggtcagga	tactctgatg	aagataaaaag	gggcttcacc	3120
aagctggtgt	atcagaacat	cttcacggcc	atgcaggcca	tgatcagagc	catggacaca	3180
ctcaagatcc	catacaagta	tgagcacaat	aaggctcatg	cacaattagt	tcgagaagtt	3240
gatgtggaga	aggtgtctgc	ttttgagaat	ccatatgtag	atgcaataaa	gagtttatgg	3300
aatgatcctg	gaatccagga	atgctatgat	agacgacgag	aatatcaatt	atctgactct	3360
accaaatact	atcttaatga	cttggaccgc	gtagctgacc	ctgcctacct	gcctacgcaa	3420
caagatgtgc	ttagagttcg	agtcccacc	acagggatca	tcgaataccc	ctttgactta	3480
caaagtgtca	ttttcagaat	ggtcgatgta	gggggccaaa	ggtcagagag	aagaaaatgg	3540
atacactgct	ttgaaaatgt	cacctctatc	atgtttctag	tagcgcttag	tgaatatgat	3600
caagttctcg	tggagtcaga	caatgagaac	cgaatggagg	aaagcaaggc	tctctttaga	3660
acaattatca	catacccctg	gttcacagaac	tcctcggtta	ttctgttctt	aaacaagaaa	3720
gatcttctag	aggagaaaat	catgtattcc	catctagtcg	actacttccc	agaatatgat	3780
ggaccccaga	gagatgccca	ggcagcccca	gaattcattc	tgaagatgtt	cgtggacctg	3840
aaccagaca	gtgacaaaat	tatctactcc	cacttcacgt	gcgccacaga	caccgagaat	3900
atccgctttg	tctttgctgc	cgtaaggac	accatcctcc	agttgaacct	gaagggtctg	3960
ggtctgtac						3969

&lt;210&gt; 45

&lt;211&gt; 1323

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

<210> 45  
 <211> 1323  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Chimeric GABA-BR $\alpha$ 1\*Gq $\alpha$ 5

<400> 45

```

Met Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1           5           10           15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
 20           25           30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
 35           40           45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
 50           55           60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65           70           75           80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
 85           90           95

Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
100          105          110

Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
115          120          125

Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
130          135          140

Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
145          150          155          160

Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
165          170          175

Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
180          185          190

Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
195          200          205

Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
210          215          220

```

Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile  
 225 230 235 240  
 Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala  
 245 250 255  
 Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro  
 260 265 270  
 Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro  
 275 280 285  
 Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp  
 290 295 300  
 Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr  
 305 310 315 320  
 Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu  
 325 330 335  
 Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys  
 340 345 350  
 Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu  
 355 360 365  
 Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe  
 370 375 380  
 Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp  
 385 390 395 400  
 Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr  
 405 410 415  
 Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro  
 420 425 430  
 Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu  
 435 440 445  
 Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe  
 450 455 460  
 Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala  
 465 470 475 480  
 Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu  
 485 490 495  
 Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala  
 500 505 510

Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp  
 515 520 525  
 Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly  
 530 535 540  
 Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu  
 545 550 555 560  
 Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp  
 565 570 575  
 Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe  
 580 585 590  
 Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val  
 595 600 605  
 Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn  
 610 615 620  
 Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala  
 625 630 635 640  
 Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg  
 645 650 655  
 Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu  
 660 665 670  
 Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val  
 675 680 685  
 His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr  
 690 695 700  
 Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met  
 705 710 715 720  
 Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg  
 725 730 735  
 Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val  
 740 745 750  
 Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr  
 755 760 765  
 Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Gly  
 770 775 780  
 Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn  
 785 790 795 800

88

Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys  
 805 810 815  
 Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala  
 820 825 830  
 Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr  
 835 840 845  
 Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly  
 850 855 860  
 Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr  
 865 870 875 880  
 Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg  
 885 890 895  
 Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu  
 900 905 910  
 Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro  
 915 920 925  
 Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu  
 930 935 940  
 Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr  
 945 950 955 960  
 Lys Ala Ala Ala Met Thr Leu Glu Ser Ile Met Ala Cys Cys Leu Ser  
 965 970 975  
 Glu Glu Ala Lys Glu Ala Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln  
 980 985 990  
 Leu Arg Arg Asp Lys Arg Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu  
 995 1000 1005  
 Leu Gly Thr Gly Glu Ser Gly Lys Ser Thr Phe Ile Lys Gln Met Arg  
 1010 1015 1020  
 Ile Ile His Gly Ser Gly Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr  
 1025 1030 1035 1040  
 Lys Leu Val Tyr Gln Asn Ile Phe Thr Ala Met Gln Ala Met Ile Arg  
 1045 1050 1055  
 Ala Met Asp Thr Leu Lys Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala  
 1060 1065 1070  
 His Ala Gln Leu Val Arg Glu Val Asp Val Glu Lys Val Ser Ala Phe  
 1075 1080 1085

Glu Asn Pro Tyr Val Asp Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly  
 1090 1095 1100  
 Ile Gln Glu Cys Tyr Asp Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser  
 1105 1110 1115 1120  
 Thr Lys Tyr Tyr Leu Asn Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr  
 1125 1130 1135  
 Leu Pro Thr Gln Gln Asp Val Leu Arg Val Arg Val Pro Thr Thr Gly  
 1140 1145 1150  
 Ile Ile Glu Tyr Pro Phe Asp Leu Gln Ser Val Ile Phe Arg Met Val  
 1155 1160 1165  
 Asp Val Gly Gly Gln Arg Ser Glu Arg Arg Lys Trp Ile His Cys Phe  
 1170 1175 1180  
 Glu Asn Val Thr Ser Ile Met Phe Leu Val Ala Leu Ser Glu Tyr Asp  
 1185 1190 1195 1200  
 Gln Val Leu Val Glu Ser Asp Asn Glu Asn Arg Met Glu Glu Ser Lys  
 1205 1210 1215  
 Ala Leu Phe Arg Thr Ile Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser  
 1220 1225 1230  
 Val Ile Leu Phe Leu Asn Lys Lys Asp Leu Leu Glu Glu Lys Ile Met  
 1235 1240 1245  
 Tyr Ser His Leu Val Asp Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg  
 1250 1255 1260  
 Asp Ala Gln Ala Ala Arg Glu Phe Ile Leu Lys Met Phe Val Asp Leu  
 1265 1270 1275 1280  
 Asn Pro Asp Ser Asp Lys Ile Ile Tyr Ser His Phe Thr Cys Ala Thr  
 1285 1290 1295  
 Asp Thr Glu Asn Ile Arg Phe Val Phe Ala Ala Val Lys Asp Thr Ile  
 1300 1305 1310  
 Leu Gln Leu Asn Leu Lys Gly Cys Gly Leu Tyr  
 1315 1320

&lt;210&gt; 46

&lt;211&gt; 4231

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Chimeric pmGluR2//CaR\*Gα<sub>i5</sub>+3Ala



&lt;400&gt; 46

atgggatcgc	tgttgcgt	cccgccactg	ctgctgctgt	ggggtgctgt	ggctgagggc	60
ccagccaaga	aggtgctgac	cctggaggga	gacttggtgc	tgggtgggct	gttcccagtg	120
caccagaagg	gcggcccagc	agaggactgt	ggctctgtca	atgagcaccg	tggcatccag	180
cgcttgagg	ccatgctttt	tgcactggac	cgcatcaacc	gtgaccgcga	cctgctgcct	240
ggcgtgcgcc	tgggtgcaca	catcctcgac	agttgctcca	aggacacaca	tgcgctggag	300
caggcactgg	actttgtgcg	tgcctcactc	agccgtgggt	ctgatggctc	acgccacatc	360
tgccccgacg	gctcttatgc	gacccatggt	gatgctccca	ctgccatcac	tgggtgttatt	420
ggcgttcct	acagtgatgt	ctccatccag	gtggccaacc	tcttgaggct	atttcagatc	480
ccacagatta	gctacgcctc	taccagtgcc	aagctgagtg	acaagtcccg	ctatgactac	540
tttggccgca	cagtgcctcc	tgacttcttc	caagccaagg	ccatggctga	gattctccgc	600
ttcttcaact	ggacctatgt	gtccactgtg	gcgtctgagg	gcgactatgg	cgagacaggc	660
attgaggcct	ttgagctaga	ggctcgtgcc	cgcaacatct	gtgtggccac	ctcggagaaa	720
gtgggcccgtg	ccatgagccg	cgcgcccttt	gaggggtgtg	tgcgagccct	gctgcagaaag	780
cccagtgcgc	gcgtggctgt	cctgttcacc	cgttctgagg	atgcccgga	gctgcttgct	840
gccagccagc	gcctcaatgc	cagcttcacc	tgggtggcca	gtgatggttg	gggggcccctg	900
gagagtgtgg	tggcaggcag	tgagggggct	gtcaggggtg	ctatcaccat	cgagtggcc	960
tcctacccca	tcagtgactt	tgccctctac	ttccagagcc	tggacccttg	gaacaacagc	1020
cggaacccct	ggttccgtga	attctgggag	cagagggtcc	gctgcagctt	ccggcagcga	1080
gactgcgcag	cccactctct	ccgggctgtg	ccctttgagc	aggagtccaa	gatcatgttt	1140
gtggtcaatg	cagtgtacgc	catggcccat	gcgctccaca	acatgcaccg	tgccctctgc	1200
cccaacacca	ccgggctctg	tgacgcgatg	cggccagtta	acggggcccg	cctctacaag	1260
gactttgtgc	tcaacgtcaa	gtttgatgcc	ccctttcgcc	cagctgacac	ccacaatgag	1320
gtccgctttg	accgctttgg	tgatgggtatt	ggccgctaca	acatcttcac	ctatctgcgt	1380
gcaggcagtg	ggcgctatcg	ctaccagaag	gtgggctact	gggcagaagg	cttgactctg	1440
gacaccagcc	tcattcccatg	ggcctcacc	tcagccggcc	cctgcccgc	ctctcgctgc	1500
agtgagccct	gcctccagaa	tgagggtgaag	agtgtgcagc	cgggcggaagt	ctgctgctgg	1560
ctctgcattc	cgtgccagcc	ctatgagtac	cgattggacg	aattcacttg	cgctgattgt	1620
ggcctggggt	actggcccaa	tgccagcctg	actggctgct	tcgaactgcc	ccaggagtac	1680
atccgctggg	gcgatgcctg	ggctgtggga	cctgtcacca	tcgcctgcct	cggtgccctg	1740
gccaccctct	ttgtgctggg	tgtctttgtg	cggcacaatg	ccacaccagt	ggtcaaggcc	1800
tcaggctggg	agctctgcta	catcctgctg	gggtggtgtc	tcctctgcta	ctgcatgacc	1860
ttcatcttca	ttgccaaagg	atccacggca	gtgtgtacct	tacggcgtct	tggtttgggc	1920
actgccttct	ctgtctgcta	ctcagccctg	ctcaccaaga	ccaaccgcac	tgacgcacatc	1980
ttcgggtggg	cccgggaggg	tgcccagcgg	ccacgcttca	tcagtcctgc	ctcacagggtg	2040
gccaactctgc	tggcacttat	ctcggggccag	ctgctcatcg	tggctgcctg	gctggtgggtg	2100
gaggcaccgg	gcacaggcaa	ggagacagcc	ccgaacggc	gggagggtgtg	gacactgcgc	2160
tgcaaccacc	gcgatgcaag	tatgttgggc	tcgctggcct	acaatgtgct	cctcatcgcg	2220
ctctgcacgc	tttatgcctt	caagactcgc	aagtgcctcg	aaaacttcaa	cgaggccaag	2280
ttcattggct	tcaccatgta	caccacctgc	atcatctggc	tggcattcct	gcccattctc	2340
tatgtcacct	ccagtgacta	ccgggtacag	accaccacca	tgtgcgtgtc	agtcagcctc	2400
agcggctccg	tgggtgcttg	ctgcctcttt	gcgcccgaag	tgacatcat	cctcttccag	2460
ccgcagaaga	acaccatcga	ggagggtgcgt	tgacgaccg	cagctcacgc	tttcaagggtg	2520
gctgcccggg	ccacgctgcg	ccgcagcaac	gtctcccga	agcgggtccag	cagccttgga	2580
ggctccacgg	gatccacccc	ctcctcctcc	atcagcagca	agagcaacag	cgaagaccca	2640
ttcccacagc	ccgagaggca	gaagcagcag	cagccgctgg	ccctaaccga	gcaagagcag	2700
cagcagcagc	ccctgaccct	cccacagcag	caacgatctc	agcagcagcc	cagatgcaag	2760
cagaagggtca	tctttggcag	cgccacggtc	accttctcac	tgagctttga	tgagcctcag	2820
aagaacgcca	tggcccacgg	gaattctacg	caccagaact	ccctggaggc	ccagaaaagc	2880
agcgatacgc	tgacccgaca	ccagccatta	ctcccgtgc	agtgcgggga	aacggactta	2940
gatctgaccg	tccaggaaac	aggtctgcaa	ggacctgtgg	gtggagacca	gcggccagag	3000
gtggaggacc	ctgaagagtt	gtccccagca	cttgtagtgt	ccagttcaca	gagctttgtc	3060
atcagtgggtg	gaggcagcac	tgttacagaa	aacgtagtga	attcagcggc	cgccatgact	3120
ctggagtcca	tcattggcgtg	ctgcctgagc	gaggaggcca	aggaagcccg	gcggatcaac	3180

```

gacgagatcg agcggcagct ccgcagggac aagcgggacg cccgccggga gctcaagctg 3240
ctgctgctcg ggacaggaga gagtggcaag agtacgttta tcaagcagat gagaatcatc 3300
catgggtcag gatactctga tgaagataaa aggggcttca ccaagctggg gtatcagaac 3360
atcttcacgg ccatgcaggc catgatcaga gccatggaca cactcaagat cccatacaag 3420
tatgagcaca ataaggctca tgcacaatta gttcgagaag ttgatgtgga gaagggtgtct 3480
gcttttgaga atccatatgt agatgcaata aagagtttat ggaatgatcc tggaatccag 3540
gaatgctatg atagacgacg agaatatcaa ttatctgact ctaccaaata ctatcttaat 3600
gacttggaac gcgtagctga ccctgcctac ctgcctacgc aacaagatgt gcttagagtt 3660
cgagtcccca ccacagggat catcgaatac ccctttgact tacaaaagtgt cattttcaga 3720
atgggtcgatg tagggggcca aaggtcagag agaagaaaat ggatacactg ctttgaanaat 3780
gtcacctcta tcatgtttct agtagcgctt agtgaatatg atcaagttct cgtggagtca 3840
gacaatgaga accgaatgga ggaaagcaag gctctcttta gaacaattat cacatacccc 3900
tgggtccaga actcctcggg tattctgttc ttaaacaaga aagatcttct agaggagaaa 3960
atcatgtatt cccatctagt cgactacttc ccagaatatg atggacccca gagagatgcc 4020
caggcagccc gagaattcat tctgaagatg ttcgtggacc tgaaccaga cagtgacaaa 4080
attatctact cccacttcac gtgcgccaca gacaccgaga atatccgctt tgtctttgct 4140
gccgtcaagg acaccatcct ccagttgaac ctgaaggact gcggtctgtt ctaattgtgc 4200
ctcctagaca cccgccctgc ccttcctggt t 4231

```

&lt;210&gt; 47

&lt;211&gt; 1397

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Chimeric pmGluR2//CaR\*Gα<sub>i5</sub>+3Ala

&lt;400&gt; 47

```

Met Gly Ser Leu Leu Ala Leu Pro Ala Leu Leu Leu Trp Gly Ala
 1              5              10              15

Val Ala Glu Gly Pro Ala Lys Lys Val Leu Thr Leu Glu Gly Asp Leu
      20              25              30

Val Leu Gly Gly Leu Phe Pro Val His Gln Lys Gly Gly Pro Ala Glu
      35              40              45

Asp Cys Gly Pro Val Asn Glu His Arg Gly Ile Gln Arg Leu Glu Ala
      50              55              60

Met Leu Phe Ala Leu Asp Arg Ile Asn Arg Asp Pro His Leu Leu Pro
      65              70              75              80

Gly Val Arg Leu Gly Ala His Ile Leu Asp Ser Cys Ser Lys Asp Thr
      85              90              95

His Ala Leu Glu Gln Ala Leu Asp Phe Val Arg Ala Ser Leu Ser Arg
      100              105              110

```

Gly Ala Asp Gly Ser Arg His Ile Cys Pro Asp Gly Ser Tyr Ala Thr  
 115 120 125  
 His Gly Asp Ala Pro Thr Ala Ile Thr Gly Val Ile Gly Gly Ser Tyr  
 130 135 140  
 Ser Asp Val Ser Ile Gln Val Ala Asn Leu Leu Arg Leu Phe Gln Ile  
 145 150 155 160  
 Pro Gln Ile Ser Tyr Ala Ser Thr Ser Ala Lys Leu Ser Asp Lys Ser  
 165 170 175  
 Arg Tyr Asp Tyr Phe Ala Arg Thr Val Pro Pro Asp Phe Phe Gln Ala  
 180 185 190  
 Lys Ala Met Ala Glu Ile Leu Arg Phe Phe Asn Trp Thr Tyr Val Ser  
 195 200 205  
 Thr Val Ala Ser Glu Gly Asp Tyr Gly Glu Thr Gly Ile Glu Ala Phe  
 210 215 220  
 Glu Leu Glu Ala Arg Ala Arg Asn Ile Cys Val Ala Thr Ser Glu Lys  
 225 230 235 240  
 Val Gly Arg Ala Met Ser Arg Ala Ala Phe Glu Gly Val Val Arg Ala  
 245 250 255  
 Leu Leu Gln Lys Pro Ser Ala Arg Val Ala Val Leu Phe Thr Arg Ser  
 260 265 270  
 Glu Asp Ala Arg Glu Leu Leu Ala Ala Ser Gln Arg Leu Asn Ala Ser  
 275 280 285  
 Phe Thr Trp Val Ala Ser Asp Gly Trp Gly Ala Leu Glu Ser Val Val  
 290 295 300  
 Ala Gly Ser Glu Gly Ala Ala Glu Gly Ala Ile Thr Ile Glu Leu Ala  
 305 310 315 320  
 Ser Tyr Pro Ile Ser Asp Phe Ala Ser Tyr Phe Gln Ser Leu Asp Pro  
 325 330 335  
 Trp Asn Asn Ser Arg Asn Pro Trp Phe Arg Glu Phe Trp Glu Gln Arg  
 340 345 350  
 Phe Arg Cys Ser Phe Arg Gln Arg Asp Cys Ala Ala His Ser Leu Arg  
 355 360 365  
 Ala Val Pro Phe Glu Gln Glu Ser Lys Ile Met Phe Val Val Asn Ala  
 370 375 380  
 Val Tyr Ala Met Ala His Ala Leu His Asn Met His Arg Ala Leu Cys  
 385 390 395 400

Pro Asn Thr Thr Arg Leu Cys Asp Ala Met Arg Pro Val Asn Gly Arg  
 405 410 415  
 Arg Leu Tyr Lys Asp Phe Val Leu Asn Val Lys Phe Asp Ala Pro Phe  
 420 425 430  
 Arg Pro Ala Asp Thr His Asn Glu Val Arg Phe Asp Arg Phe Gly Asp  
 435 440 445  
 Gly Ile Gly Arg Tyr Asn Ile Phe Thr Tyr Leu Arg Ala Gly Ser Gly  
 450 455 460  
 Arg Tyr Arg Tyr Gln Lys Val Gly Tyr Trp Ala Glu Gly Leu Thr Leu  
 465 470 475 480  
 Asp Thr Ser Leu Ile Pro Trp Ala Ser Pro Ser Ala Gly Pro Leu Pro  
 485 490 495  
 Ala Ser Arg Cys Ser Glu Pro Cys Leu Gln Asn Glu Val Lys Ser Val  
 500 505 510  
 Gln Pro Gly Glu Val Cys Cys Trp Leu Cys Ile Pro Cys Gln Pro Tyr  
 515 520 525  
 Glu Tyr Arg Leu Asp Glu Phe Thr Cys Ala Asp Cys Gly Leu Gly Tyr  
 530 535 540  
 Trp Pro Asn Ala Ser Leu Thr Gly Cys Phe Glu Leu Pro Gln Glu Tyr  
 545 550 555 560  
 Ile Arg Trp Gly Asp Ala Trp Ala Val Gly Pro Val Thr Ile Ala Cys  
 565 570 575  
 Leu Gly Ala Leu Ala Thr Leu Phe Val Leu Gly Val Phe Val Arg His  
 580 585 590  
 Asn Ala Thr Pro Val Val Lys Ala Ser Gly Arg Glu Leu Cys Tyr Ile  
 595 600 605  
 Leu Leu Gly Gly Val Phe Leu Cys Tyr Cys Met Thr Phe Ile Phe Ile  
 610 615 620  
 Ala Lys Pro Ser Thr Ala Val Cys Thr Leu Arg Arg Leu Gly Leu Gly  
 625 630 635 640  
 Thr Ala Phe Ser Val Cys Tyr Ser Ala Leu Leu Thr Lys Thr Asn Arg  
 645 650 655  
 Ile Ala Arg Ile Phe Gly Gly Ala Arg Glu Gly Ala Gln Arg Pro Arg  
 660 665 670  
 Phe Ile Ser Pro Ala Ser Gln Val Ala Ile Cys Leu Ala Leu Ile Ser  
 675 680 685

Gly Gln Leu Leu Ile Val Val Ala Trp Leu Val Val Glu Ala Pro Gly  
 690 695 700  
 Thr Gly Lys Glu Thr Ala Pro Glu Arg Arg Glu Val Val Thr Leu Arg  
 705 710 715 720  
 Cys Asn His Arg Asp Ala Ser Met Leu Gly Ser Leu Ala Tyr Asn Val  
 725 730 735  
 Leu Leu Ile Ala Leu Cys Thr Leu Tyr Ala Phe Lys Thr Arg Lys Cys  
 740 745 750  
 Pro Glu Asn Phe Asn Glu Ala Lys Phe Ile Gly Phe Thr Met Tyr Thr  
 755 760 765  
 Thr Cys Ile Ile Trp Leu Ala Phe Leu Pro Ile Phe Tyr Val Thr Ser  
 770 775 780  
 Ser Asp Tyr Arg Val Gln Thr Thr Thr Met Cys Val Ser Val Ser Leu  
 785 790 795 800  
 Ser Gly Ser Val Val Leu Gly Cys Leu Phe Ala Pro Lys Leu His Ile  
 805 810 815  
 Ile Leu Phe Gln Pro Gln Lys Asn Thr Ile Glu Glu Val Arg Cys Ser  
 820 825 830  
 Thr Ala Ala His Ala Phe Lys Val Ala Ala Arg Ala Thr Leu Arg Arg  
 835 840 845  
 Ser Asn Val Ser Arg Lys Arg Ser Ser Ser Leu Gly Gly Ser Thr Gly  
 850 855 860  
 Ser Thr Pro Ser Ser Ser Ile Ser Ser Lys Ser Asn Ser Glu Asp Pro  
 865 870 875 880  
 Phe Pro Gln Pro Glu Arg Gln Lys Gln Gln Gln Pro Leu Ala Leu Thr  
 885 890 895  
 Gln Gln Glu Gln Gln Gln Gln Pro Leu Thr Leu Pro Gln Gln Gln Arg  
 900 905 910  
 Ser Gln Gln Gln Pro Arg Cys Lys Gln Lys Val Ile Phe Gly Ser Gly  
 915 920 925  
 Thr Val Thr Phe Ser Leu Ser Phe Asp Glu Pro Gln Lys Asn Ala Met  
 930 935 940  
 Ala His Gly Asn Ser Thr His Gln Asn Ser Leu Glu Ala Gln Lys Ser  
 945 950 955 960  
 Ser Asp Thr Leu Thr Arg His Gln Pro Leu Leu Pro Leu Gln Cys Gly  
 965 970 975

Glu Thr Asp Leu Asp Leu Thr Val Gln Glu Thr Gly Leu Gln Gly Pro  
 980 985 990  
 Val Gly Gly Asp Gln Arg Pro Glu Val Glu Asp Pro Glu Glu Leu Ser  
 995 1000 1005  
 Pro Ala Leu Val Val Ser Ser Ser Gln Ser Phe Val Ile Ser Gly Gly  
 1010 1015 1020  
 Gly Ser Thr Val Thr Glu Asn Val Val Asn Ser Ala Ala Ala Met Thr  
 1025 1030 1035 1040  
 Leu Glu Ser Ile Met Ala Cys Cys Leu Ser Glu Glu Ala Lys Glu Ala  
 1045 1050 1055  
 Arg Arg Ile Asn Asp Glu Ile Glu Arg Gln Leu Arg Arg Asp Lys Arg  
 1060 1065 1070  
 Asp Ala Arg Arg Glu Leu Lys Leu Leu Leu Gly Thr Gly Glu Ser  
 1075 1080 1085  
 Gly Lys Ser Thr Phe Ile Lys Gln Met Arg Ile Ile His Gly Ser Gly  
 1090 1095 1100  
 Tyr Ser Asp Glu Asp Lys Arg Gly Phe Thr Lys Leu Val Tyr Gln Asn  
 1105 1110 1115 1120  
 Ile Phe Thr Ala Met Gln Ala Met Ile Arg Ala Met Asp Thr Leu Lys  
 1125 1130 1135  
 Ile Pro Tyr Lys Tyr Glu His Asn Lys Ala His Ala Gln Leu Val Arg  
 1140 1145 1150  
 Glu Val Asp Val Glu Lys Val Ser Ala Phe Glu Asn Pro Tyr Val Asp  
 1155 1160 1165  
 Ala Ile Lys Ser Leu Trp Asn Asp Pro Gly Ile Gln Glu Cys Tyr Asp  
 1170 1175 1180  
 Arg Arg Arg Glu Tyr Gln Leu Ser Asp Ser Thr Lys Tyr Tyr Leu Asn  
 1185 1190 1195 1200  
 Asp Leu Asp Arg Val Ala Asp Pro Ala Tyr Leu Pro Thr Gln Gln Asp  
 1205 1210 1215  
 Val Leu Arg Val Arg Val Pro Thr Thr Gly Ile Ile Glu Tyr Pro Phe  
 1220 1225 1230  
 Asp Leu Gln Ser Val Ile Phe Arg Met Val Asp Val Gly Gly Gln Arg  
 1235 1240 1245  
 Ser Glu Arg Arg Lys Trp Ile His Cys Phe Glu Asn Val Thr Ser Ile  
 1250 1255 1260

Met Phe Leu Val Ala Leu Ser Glu Tyr Asp Gln Val Leu Val Glu Ser  
1265 1270 1275 1280

Asp Asn Glu Asn Arg Met Glu Glu Ser Lys Ala Leu Phe Arg Thr Ile  
1285 1290 1295

Ile Thr Tyr Pro Trp Phe Gln Asn Ser Ser Val Ile Leu Phe Leu Asn  
1300 1305 1310

Lys Lys Asp Leu Leu Glu Glu Lys Ile Met Tyr Ser His Leu Val Asp  
1315 1320 1325

Tyr Phe Pro Glu Tyr Asp Gly Pro Gln Arg Asp Ala Gln Ala Ala Arg  
1330 1335 1340

Glu Phe Ile Leu Lys Met Phe Val Asp Leu Asn Pro Asp Ser Asp Lys  
1345 1350 1355 1360

Ile Ile Tyr Ser His Phe Thr Cys Ala Thr Asp Thr Glu Asn Ile Arg  
1365 1370 1375

Phe Val Phe Ala Ala Val Lys Asp Thr Ile Leu Gln Leu Asn Leu Lys  
1380 1385 1390

Asp Cys Gly Leu Phe  
1395

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/07333

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 6 C07K14/705 C12N15/12 C12N15/62 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 05252 A (NPS PHARMA INC) 13 February 1997 (1997-02-13) cited in the application see the whole document and specially pages 59-60.	13-28, 33,38,40
Y	WO 97 46675 A (NOVARTIS AG) 11 December 1997 (1997-12-11) cited in the application page 2, last paragraph - page 3, paragraph 1 page 50-56 page 62-67 page 86-90	13-28, 33,38,39

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

**Special categories of cited documents:**

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Δ\* document member of the same patent family

Date of the actual completion of the international search

13 September 1999

Date of mailing of the international search report

28/09/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
 Fax: (+31-70) 340-3016

Authorized officer

Mateo Rosell, A.M.



# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/07333

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KAUPMANN K ET AL: "EXPRESSION CLONING OF GABAB RECEPTORS UNCOVERS SIMILARITY TO METABOTROPIC GLUTAMATE RECEPTORS" NATURE, vol. 386, no. 6622, 20 March 1997 (1997-03-20), pages 239-246, XP002032306 ISSN: 0028-0836 see the whole document and specially Fig.3 ---	13-28, 33
Y	WO 97 48724 A (NPS PHARMA INC) 24 December 1997 (1997-12-24) cited in the application figure 1 ---	13-28, 33, 38, 40
Y	EP 0 816 498 A (LILLY CO ELI) 7 January 1998 (1998-01-07) abstract page 21, line 35-58 page 46-48 ---	13-28, 33, 38, 39
X	WO 97 48820 A (AURORA BIOSCIENCES CORP) 24 December 1997 (1997-12-24) page 3, line 1-4 page 46-53 ---	5, 32
A	WO 92 05244 A (UNIV DUKE) 2 April 1992 (1992-04-02) page 2, line 15-25 page 4, line 20-34 page 10, line 25-36; examples 4, 5 ---	1, 5, 8-10
A	B. BERTIN ET AL., : "Cellular signaling by agonist-activated receptor/Gsalpha fusion protein" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 91, 1994, pages 8827-8831, XP002114989 cited in the application the whole document ---	1, 5, 8-10
A	A. WISE AND G. MILLIGAN : "Rescue of functional interactions between the alpha2A-adrenoreceptor and acylation-resistant forms of Gialpha by expressing the proteins from chimeric open reading frames" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 39, 1997, pages 24673-24678, XP002114990 cited in the application abstract page 24676, paragraph 3 ---	1, 38-40
	-/--	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/07333

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 99 20751 A (BOROWSKY BETH ; JONES KENNETH A (US); LAZ THOMAS M (US); SYNAPTIC P) 29 April 1999 (1999-04-29) abstract page 105-109; table 3 figures 2A-D -----</p>	<p>13-28, 38, 39</p>

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/07333

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9705252	A	13-02-1997	AU 6602296 A CA 2200606 A EP 0783577 A JP 10507934 T	26-02-1997 13-02-1997 16-07-1997 04-08-1998
WO 9746675	A	11-12-1997	AU 2028497 A CA 2254862 A EP 0907731 A	05-01-1998 11-12-1997 14-04-1999
WO 9748724	A	24-12-1997	AU 3715697 A CA 2246751 A EP 0882065 A	07-01-1998 24-12-1997 09-12-1998
EP 0816498	A	07-01-1998	NONE	
WO 9748820	A	24-12-1997	AU 3572897 A	07-01-1998
WO 9205244	A	02-04-1992	AU 652576 B AU 8511591 A CA 2092717 A EP 0548165 A JP 6500693 T US 5482835 A US 5739029 A	01-09-1994 15-04-1992 14-03-1992 30-06-1993 27-01-1994 09-01-1996 14-04-1998
WO 9920751	A	29-04-1999	AU 1101099 A	10-05-1999